Scientific and Technical Information Center

S	EARCH REQUEST	Γ FORM	
Art Unit: 1016 Phone N Location (Bldg/Room#): (M ************************************	Stailbox #): 4 C FO Results F		
Title of Invention: Pro Cors Inventors (please provide full names):	of Pref. of 1-	3-(dimethylamicus) profug -1-4	ľ.
Raja	mannas.	et=(
Earliest Priority Date:	mannas 9 7/2002 (37	71)	
Search Topic: Please provide a detailed statement of the search	ch topic, and describe as specifically as ms, acronyms, and registry numbers, a	s possible the subject matter to be searched. Include the and combine with the concept or utility of the invention.	
appropriate serial number. 1-3,5	- 22, , 41-42, 49		
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Searcher Phone #:	AA Sequence (#)	Questel/Orbit Lexis/Nexis	
Searcher Location:	Structure (#)	Westlaw WWW/Internet	
Date Searcher Picked Up: 6/19/06	Bibliographic	In-house sequence systems	
Date Completed: 6/19/06	Litigation	CommercialOligomerScore/LengthInterferenceSPDIEncode/TranslOther (specify)	
Searcher Prep & Review Time:	Fulltext		

PATENT ASSIGNEE(S):

Pharmachem Technologies Limited, UK

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT	NO.			KIN	D	DATE	;		APP	LICAT	CION	NO.		D	ATE	
WO	2003	0292	 36				2003	0410			2002-				-		
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		FI,	FR,	GB,	GR,	IE,	IT.	LU.	MC.	NT.	, en,	CI,	CZ,	DΕ,	DK,	EE,	ES,
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CA	24612	213			AA		2003	0410		CA :	2002-	2461	212		2.		
EP	1470	744			AT		20041	0623	1	FD 1	2002-	77911	^ 2		~ .		
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OTHER SO	URCE (S):			CASR	EAC	r 138	. 305	791		.002-1	JE T 0 C	743	W	20	0209	23

OTHER SOURCE(S): CASREACT 138:305791

AB The present invention provides a process for the preparation of Citalopram, a known antidepressant.

IT 59729-32-7P 59729-33-8P, Citalopram 64169-39-7P RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(process for the preparation of citalopram and derivs.)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$NC$$
 O $(CH2)3-NMe2$

HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:172971 CAPLUS

DOCUMENT NUMBER:

138:221462

TITLE:

Improved process for the manufacture of citalogram $% \left(1\right) =\left(1\right) \left(1\right) \left($

hydrobromide from 5-bromophthalide

PATENT ASSIGNEE(S):

Sekhsaria Chemicals Ltd., India

SOURCE:

Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

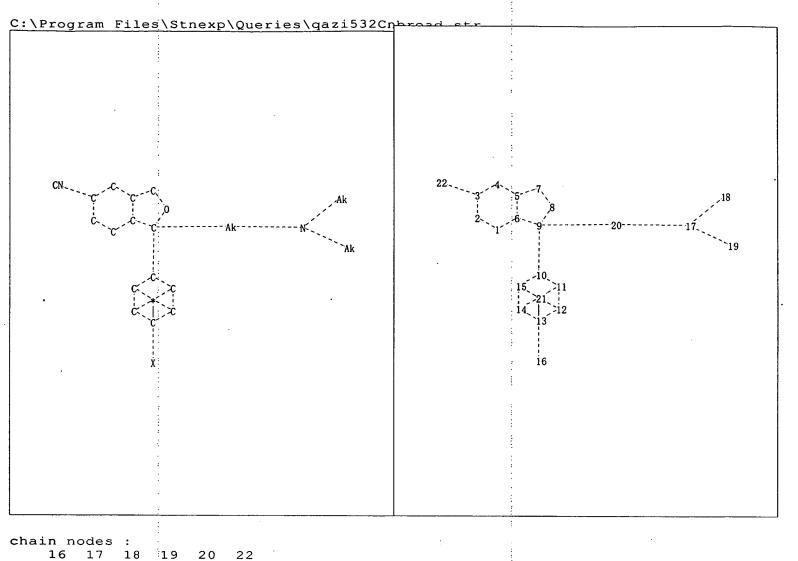
LANGUAGE:

T: 1

FAMILY ACC. NUM. COUNT:

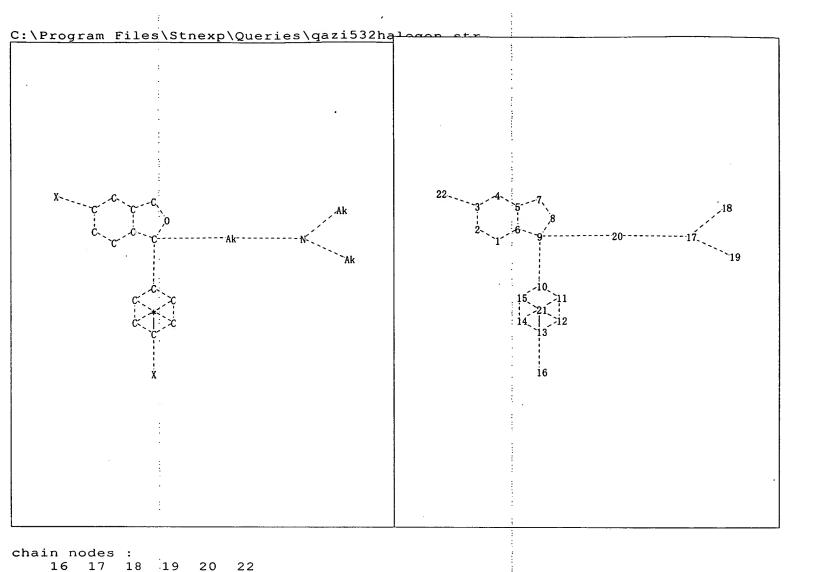
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288211	A1	20030305	EP 2002-255750	20020819



ring nodes : 1 2 3 4 5 6 7 9 10 11 8 12 13 14 chain bonds : 3-22 9-10 9-20 17-19 17-18 17-20 ring bonds : 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14 14-15 exact/norm bonds : 1-2 1-6 2-3 3-4 3-22 4-5 5-6 5-7 6-9 7-8 8-9 9-10 9-20 10-11 $10 - 15 \quad 11 - 12 \quad 12 - 13 \quad 13 - 14 \quad 14 - 15 \quad 17 - 19 \quad 17 - 18 \quad 17 - 20$ Match level :

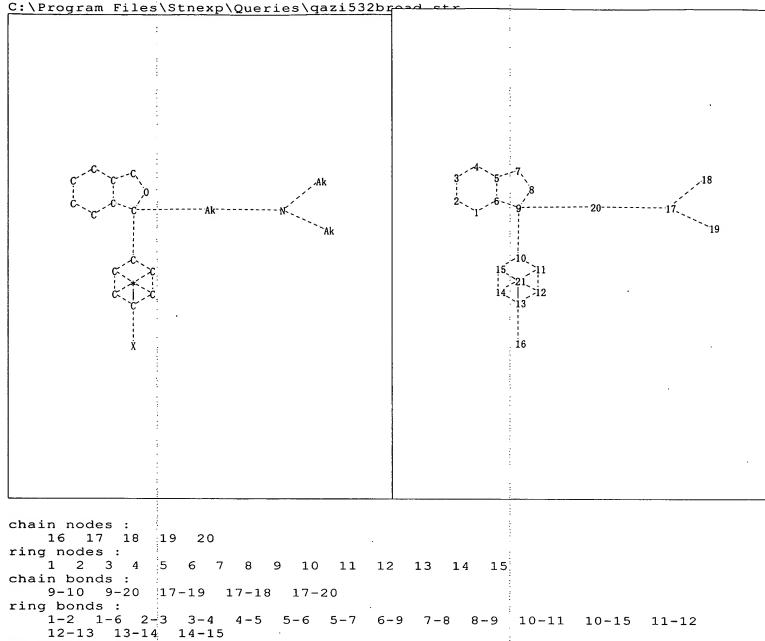
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS



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ring nodes :
   1 2 3 4
               5
                            9 10
                                   11
                                       12
                                           13
                                              14 15
chain bonds :
               9-20 17-19
    3-22 9-10
                            17-18
ring bonds :
    1-2 1-6 2-3 3-4 4-5
                             5-6 5-7
                                       6-9
                                           7-8
                                                 8-9
                                                      10-11
    12-13 13-14 14-15
exact/norm bonds :
   1-2 1-6 2-3 3-4 3-22 4-5 5-6 5-7 6-9 7-8 8-9 10-15 11-12 12-13 13-14 14-15 17-19 17-18 17-20
                                                            9-10 9-20 10-11
Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom
    10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS
                                                                     17:CLASS
    18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
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chain bonds :
 9-10 9-20 17-19 17-18 17-20
ring bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12
 12-13 13-14 14-15
exact/norm bonds :
 1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 9-10 9-20 10-11 10-15
 11-12 12-13 13-14 14-15 17-19 17-18 17-20

Match level :
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS

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FILE 'CAPLUS' ENTERED AT 14:03:44 ON 19 JUN 2006 E US2004-500532/APPS

- L1 1 SEA ABB=ON PLU=ON US2004-500532/AP D BROWSE
 - E RAJAMANNAR T/AU
- 21 SEA ABB=ON PLU=ON ("RAJAMANNAR T"/AU OR "RAJAMANNAR THENNATI" L2
 - E SRINIVASU K/AU
- 6 SEA ABB=ON PLU=ON "SRINIVASU K"/AU L3E PATEL N/AU
- 184 SEA ABB=ON PLU=ON ("PATEL N"/AU OR "PATEL N S"/AU OR "PATEL L4N S A"/AU OR "PATEL NAME NOT TRANSLATED"/AU OR "PATEL NILESH"/A U OR "PATEL NILESHKUMAR"/AU OR "PATEL NILESHKUMAR SURESHBAI"/AU OR "PATEL NILESHKUMAR SURESHBHAI"/AU) E RAJENDRAN C/AU
- 13 SEA ABB=ON PLU=ON ("RAJENDRAN C"/AU OR "RAJENDRAN C P"/AU OR L5 "RAJENDRAN C PANCHAPAKESA"/AU)
- O SEA ABB=ON PLU=ON (L2 AND (L3 OR L4 OR L5)) OR (L3 AND (L4 L6 OR L5)) OR (L4 AND L5)
- 224 SEA ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5) L7
- 1 SEA ABB=ON PLU=ON L7 AND L1 L8 E SUN /CS, PA
- 1 SEA ABB=ON PLU=ON ("SUN A PHARM CO LTD"/CS OR "SUN A PHARM L9 CO LTD"/PA OR "SUN A PHARM CO LTD JAPAN"/CS OR "SUN A PHARM CO LTD JAPAN"/PA)
 - E SUN P/CS.PA
 - E SUN PHARM?/CS,PA
- L10 434 SEA ABB=ON PLU=ON SUN PHARM?/CS,PA D BIB
 - D BIB 3
- O SEA ABB=ON PLU=ON SUN/OBI (1W) PHARM?/CS,PA L11
 - E SUB PHARM/AU
 - E SUB PHARM/CS, PA
 - E SUN PHARM/CS, PA
- L12 96 SEA ABB=ON PLU=ON ("SUN PHARM CORP POMPANO BEACH FL USA"/CS OR "SUN PHARM IND VADODARA 390 007 INDIA"/CS OR "SUN PHARM LTD POMPANO BEACH FL USA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER BARODA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER VADODARA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RES CENT AKOTA GUJARAT INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE AKOTA VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA 390 020 GJ INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA GUJARAL 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUTICAL CORP"/CS OR "SUN PHARMACEUTICAL CORP"/PA OR "SUN PHARMACEUTICAL CORP USA"/CS OR "SUN PHARMACEUTICAL CORP USA"/PA OR "SUN PHARMACEUTICAL IND LTD"/CS OR "SUN PHARMACEUTICAL IND LTD"/PA OR "SUN PHARMACEUTICAL IND LTD INDIA"/CS OR "SUN PHARMACEUTICAL IND LTD INDIA"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/C S OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED INDIA"/CS OR "SUN PHARMACEUTI CAL INDUSTRIES LIMITED INDIA"/PA OR "SUN PHARMACEUTICAL

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INDUSTRIES LTD"/CS OR "SUN PHARMACEUTICAL INDUSTRIES LTD"/PA
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PHARMACEUTICALS INDUSTRIES LTD INDIA"/CS OR "SUN PHARMACEUTICAL
S INDUSTRIES LTD INDIA"/PA)
SEA ABB=ON PLU=ON L10 AND L12
SEA ABB=ON PLU=ON L13 AND (L1 OR L2 OR L3 OR L4 OR L5)

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96 SEA ABB=ON PLU=ON L10 AND L12
11 SEA ABB=ON PLU=ON L13 AND (L1 OR L2 OR L3 OR L4 OR L5)
L13
L14
                    E CITALOPRAM/CT
                    E E3+ALL
            1720 SEA ABB=ON PLU=ON CITALOPRAM+PFT/CT
15343 SEA ABB=ON PLU=ON (BENZOFURAN?)/OBI,BI
2355 SEA ABB=ON PLU=ON (CITALOPRAM?)/OBI,BI
3 SEA ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4 OR L5 OR L13) AND
L15
L16
L17
L18
                     (L15 OR L16 OR L17)
      FILE 'REGISTRY' ENTERED AT 14:21:48 ON 19 JUN 2006
L19
                    STRUCTURE UPLOADED
                  5 SEA SSS SAM L19
L20
                    D OUE L19
               385 SEA SSS FUL L19
L21
      FILE 'CAPLUS' ENTERED AT 14:24:11 ON 19 JUN 2006
              1889 SEA ABB=ON PLU=ON L21
1825 SEA ABB=ON PLU=ON L22 AND (L15 OR L16 OR L17)
1025 SEA ABB=ON PLU=ON L23 NOT (PY>2002 OR PRY>2002 OR AY>2002)
L22
L23
L24
      FILE 'STNGUIDE' ENTERED AT 14:27:10 ON 19 JUN 2006
      FILE 'REGISTRY' ENTERED AT 14:28:52 ON 19 JUN 2006
L25
                   STRUCTURE UPLOADED
L26
                20 SEA SSS SAM L25
                20 SEA SUB=L21 SSS SAM L25
L27
L28
               351 SEA SUB=L21 SSS FUL L25
L29
                    STRUCTURE UPLOADED
L30
                11 SEA SUB=L21 SSS SAM L29
L31
               207 SEA SUB=L21 SSS FUL L29
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      FILE 'REGISTRY' ENTERED AT 14:33:10 ON 19 JUN 2006
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FILE 'CAPLUS' ENTERED AT 14:33:26 ON 19 JUN 2006 L32 1887 SEA ABB=ON PLU=ON L31

L33 ANALYZE PLU=ON L32 1-1887 RN : 15932 TERMS

FILE 'CAPLUS' ENTERED AT 14:35:45 ON 19 JUN 2006 L35 1720 SEA ABB=ON PLU=ON L34

FILE 'REGISTRY' ENTERED AT 14:36:52 ON 19 JUN 2006

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D QUE L25
L36
                STRUCTURE UPLOADED
                STRUCTURE UPLOADED
L37
              1 SEA SUB=L21 SSS SAM L36
L38
                D SCAN
L39
             49 SEA SUB=L21 SSS FUL L36
             10 SEA SUB=L21 SSS SAM L37
L40
            180 SEA SUB=L21 SSS FUL L37
L41
     FILE 'CAPLUS' ENTERED AT 14:42:04 ON 19 JUN 2006
L42
            115 SEA ABB=ON PLU=ON L41 (L) PREP+ALL/RL
L43
             26 SEA ABB=ON
                            PLU=ON
                                   L39 (L) RACT+ALL/RL
L44
             25 SEA ABB=ON
                            PLU=ON
                                   L42 AND L43
L45
             25 SEA ABB=ON
                           PLU=ON
                                    (L44 OR L1)
     FILE 'REGISTRY' ENTERED AT 14:43:56 ON 19 JUN 2006
                E CITALOPRAM/CN
L46
              1 SEA ABB=ON PLU=ON CITALOPRAM/CN
                D SCAN
     FILE 'BEILSTEIN' ENTERED AT 14:44:54 ON 19 JUN 2006
L47
              9 SEA SSS FUL L36
L48
             15 SEA SSS FUL L37
                SEL L47 BRN
              2 SEA ABB=ON PLU=ON (1393707/RX.RBRN OR 1393708/RX.RBRN OR
L49
                1393784/RX.RBRN OR 1436009/RX.RBRN OR 1436010/RX.RBRN OR
                1436012/RX.RBRN OR 1436013/RX.RBRN OR 1436014/RX.RBRN OR
                1437155/RX.RBRN)
                SEL BRN L48
L*** DEL
             15 S E10-E24
              8 SEA ABB=ON PLU=ON (10025981/RX.PBRN OR 10027939/RX.PBRN OR
L50
                10027940/RX.PBRN OR 10034335/RX.PBRN OR 1397373/RX.PBRN OR
                1397374/RX.PBRN OR 1397419/RX.PBRN OR 4092181/RX.PBRN OR
                5368282/RX.PBRN OR 8457580/RX.PBRN OR 8459631/RX.PBRN OR
                9001443/RX.PBRN OR 9001444/RX.PBRN OR 9826316/RX.PBRN OR
                9826317/RX.PBRN)
L51
              O SEA ABB=ON
                           PLU=ON
                                    L49 AND L50
L52
             10 SEA ABB=ON
                           PLU=ON
                                    (L49 OR L50)
     FILE 'STNGUIDE' ENTERED AT 14:49:16 ON 19 JUN 2006
     FILE 'BEILSTEIN' ENTERED AT 14:55:39 ON 19 JUN 2006
                D L50 1
     FILE 'CAPLUS' ENTERED AT 14:56:55 ON 19 JUN 2006
L53
             12 SEA ABB=ON PLU=ON
                                    (L14 OR L18)
L54
              3 SEA ABB=ON PLU=ON L45 NOT (PY>2002 OR PRY>2002 OR AY>2002)
L55
           1824 SEA ABB=ON PLU=ON L32 AND (L15 OR L16 OR L17)
=> file caplus
FILE 'CAPLUS' ENTERED AT 15:01:02 ON 19 JUN 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que 153 1 SEA FILE=CAPLUS ABB=ON PLU=ON US2004-500532/AP L1L221 SEA FILE=CAPLUS ABB=ON PLU=ON ("RAJAMANNAR T"/AU OR "RAJAMANN AR THENNATI"/AU) 6 SEA FILE=CAPLUS ABB=ON PLU=ON "SRINIVASU K"/AU 1.3 T.4 184 SEA FILE=CAPLUS ABB=ON PLU=ON ("PATEL N"/AU OR "PATEL N S"/AU OR "PATEL N S A"/AU OR "PATEL NAME NOT TRANSLATED"/AU OR "PATEL NILESH"/AU OR "PATEL NILESHKUMAR"/AU OR "PATEL NILESHKUM AR SURESHBAI"/AU OR "PATEL NILESHKUMAR SURESHBHAI"/AU) L_5 13 SEA FILE=CAPLUS ABB=ON PLU=ON ("RAJENDRAN C"/AU OR "RAJENDRAN C P"/AU OR "RAJENDRAN C PANCHAPAKESA"/AU) L10 434 SEA FILE=CAPLUS ABB=ON PLU=ON SUN PHARM?/CS,PA 96 SEA FILE=CAPLUS ABB=ON PLU=ON ("SUN PHARM CORP POMPANO BEACH L12 FL USA"/CS OR "SUN PHARM IND VADODARA 390 007 INDIA"/CS OR "SUN PHARM LTD POMPANO BEACH FL USA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER BARODA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCE RESEARCH CENTER VADODARA 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RES CENT AKOTA GUJARAT INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE AKOTA VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA 390 020 GJ INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA GUJARAL 390 020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE BARODA INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA 390020 INDIA"/CS OR "SUN PHARMA ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUTICAL CORP"/CS OR "SUN PHARMACEUTICAL CORP"/PA OR "SUN PHARMACEUTICAL CORP USA"/CS OR "SUN PHARMACEUTICAL CORP USA"/PA OR "SUN PHARMACEUTICAL IND LTD"/CS OR "SUN PHARMACEUTICAL IND LTD"/PA OR "SUN PHARMACEUTICAL IND LTD INDIA"/CS OR "SUN PHARMACEUTICAL IND LTD INDIA"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/C S OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LIMITED INDIA"/CS OR "SUN PHARMACEUTI CAL INDUSTRIES LIMITED INDIA"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LTD"/CS OR "SUN PHARMACEUTICAL INDUSTRIES LTD"/PA OR "SUN PHARMACEUTICAL INDUSTRIES LTD INDIA"/CS OR "SUN PHARMACEUTICAL INDUSTRIES LTD INDIA"/PA OR "SUN PHARMACEUTICALS ADVANCED RESEARCH CENTRE VADODARA INDIA"/CS OR "SUN PHARMACEUT ICALS CORPORATION"/CS OR "SUN PHARMACEUTICALS CORPORATION"/PA OR "SUN PHARMACEUTICALS CORPORATION USA"/CS OR "SUN PHARMACEUTI

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L13
             96 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L10 AND L12
L14
             11 SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L13 AND (L1 OR L2 OR L3 OR L4
                OR L5)
L15
          1720 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                CITALOPRAM+PFT/CT
          15343 SEA FILE=CAPLUS ABB=ON
1.16
                                        PLU=ON
                                                (BENZOFURAN?) / OBI, BI
L17
          2355 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                (CITALOPRAM?) /OBI, BI
L18
              3 SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                (L1 OR L2 OR L3 OR L4 OR L5 OR
                L13) AND (L15 OR L16 OR L17)
            12 SEA FILE=CAPLUS ABB=ON PLU=ON
L53
                                                (L14 OR L18)
=> d ibib abs 153 tot
L53 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
                         2006:380769 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         144:412891
TITLE:
                         Preparation of aminocycloalkanedicarboxylic acids and
                         related compounds as immunosuppressive agents
INVENTOR (S):
                         Capet, Marc; Levoin, Nicolas; Berrebi-Bertrand,
                         Isabelle; Poupardin, Olivia; Robert, Philippe;
                         Schwartz, Jean-Charles; Lecomte, Jeanne-Marie;
                         Rajamannar, Thennati; Pal, Ranjan Kumar;
                         Samanta, Biswajit; Jivani, Jignesh K.; Panchal,
                         Bhavesh M.; Bhatt, Isha H.; Aradhye, Jayraj D.
PATENT ASSIGNEE(S):
                         Bioprojet, Fr.; Sun Pharmaceuticals Industries
                         Ltd.
SOURCE:
                         Eur. Pat. Appl., 39 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                        KIND
                                           APPLICATION NO.
                               DATE
                                                                   DATE
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                        _ _ _ _
                               -----
                                           ------
                                                                   -----
     EP 1650186
                               20060426
                                         EP 2004-292517
                         A1
                                                                   20041022
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     WO 2006043149
                               20060427
                                           WO 2005-IB3113
                         A2
                                                                   20051018
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
            NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
            SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
            YU, ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
            IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:
                                            EP 2004-292517
                                                                A 20041022
     The invention relates to amino dicarboxylic acid derivs.
     Ar1-Y10-1-X0-1-Ar20-1-Y2-NR'-Y30-1-Z(CO2R'')COR''' [Ar1, Ar2 are
```

AB The invention relates to amino dicarboxylic acid derivs.

Ar1-Y10-1-X0-1-Ar20-1-Y2-NR'-Y30-1-Z(CO2R'')COR''' [Ar1, Ar2 are

(un)substituted aryl; Y1, Y2, Y3 are (un)substituted alkyl chains; X is a heteroatom; R', R'' are independently H or an (un)substituted alkyl chain; R''' is OH, alkoxy, H, an amino group, a natural or synthetic amino acid; Z is cycloalkyl, heterocyclyl, aryl, heteroaryl, CH, C-alkyl or Z and R' may form a ring; CO2R'' and COR''' are attached to the same atom or

Saloni Sharma 06/19/2006

adjacent atoms] which display agonistic activity at sphingosine-1phosphate (S1P) receptors for use as immunosuppressive agents. Thus, 3-(4-nonylbenzylamino)cyclopentane-1,1-dicarboxylic acid was prepared and shown to activate the S1P1 receptor (EC50 = 6) nM.

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2006:194068 CAPLUS

DOCUMENT NUMBER:

144:274127

TITLE:

Process for preparation of citalogram and

its enantiomers via acid or base cyclization of the

diol

INVENTOR(S):

Periyandi, Nagarajan; Kilaru, Srinivasu; Thennati,

Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Limited, India

SOURCE:

PCT Int. Appl., 31 pp.

GI

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	PATENT NO.				KIND DATE		APPLICATION NO.						DATE				
						_								- -			
WO	2006	0219	71		A2	:	2006	0302	WO 2005-IN276						20050812		
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KP,	KR,	KZ,
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,
		NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,
		SL,	SM,	SY,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,
		ZA,	ZM,	zw													
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,
		IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ.,
		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG,	BW,	GH,
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	ΚZ,	MD,	RU,	TJ,	TM										
PRIORITY	PRIORITY APPLN. INFO.:			.:	IN 2004-MU912			2	A 20040823								
OTHER SOURCE(S):				MAR	MARPAT 144:274127												

II

The invention provides a process for preparation of 1-[3-(dimethylamino)propyl]-

1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofurancarbonitrile I (Z = CN;citalopram) and its enantiomers. The process for preparation of compound I comprising reacting a compound of formula II (R = H), in the presence of a base, with a compound of formula RX, wherein R is (un) substituted alkyl, (un) substituted alkenyl, and (un) substituted (hetero) aryl; X is from F, Cl, Br, I, CN, OTf and OR1; R1 is (un) substituted alkyl; Z is CN or a group that may be converted to a cyano group; so that an intermediate ether derivative, where R is as defined above, is formed from said reaction, which ether cyclizes to give a compound of formula I, where Z is not a cyano group, and conversion of the group Z in the compound of formula I to a cyano group to form racemic I (Z = CN), is claimed in this invention. invention also provides ether compds., compds. of formula II and a process for preparation thereof. (S)-(+)-Citropram, i.e., (S)-(+)-I (Z = CN) was prepared by nucleophilic aromatic substitution of 2,5-dichloronitrobenzene with (S)-(-)-II (Z = CN; R = H) to give the corresponding benzylic Ph ether, that was converted to its HCl salt, and cyclized in the presence of potassium carbonate to give (S)-(+)-I.

L53 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1355587 CAPLUS

DOCUMENT NUMBER: 144:74891

TITLE: Novel stable polymorphic forms of tiagabine

hydrochloride

INVENTOR(S): Natarajan, Muthukumaran; Patel, Nileshkumar

Sureshbhai; Bhatt, Mehul Chandrakatbhai; Kilaru,

Srinivasu; Thennati, Rajamannar

PATENT ASSIGNEE(S): Sun Phar

SOURCE:

Sun Pharmaceutical Industries Limited, India

PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:
FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APP				APPLICATION NO. DATE														
WO 2005122698 A			A2	A2 20051229			1	WO 2004-IN447					20041224					
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	
		SY,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	zw
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IS,	IT,	LT,	LU,	MC,	NL,	PL,	PT,	
		RO,	SE,	SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	
		MR,	NE,	SN,	TD,	TG												

PRIORITY APPLN. INFO.:

IN 2003-MU1210 A 20031224

AB Stable polymorphic forms III, IV and substantially amorphous forms of an anticonvulsant, tiagabine-HCl. Thus, a monoacetonitrile solvate of tiagabine-HCl was prepared by the reaction of the drug hydrochloride with MeCN. The solvate was characterized by x-ray diffraction.

L53 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:294515 CAPLUS

DOCUMENT NUMBER: 142:316575

TITLE: A process for the preparation of iopamidol in a

pharmaceutically acceptable form

INVENTOR(S): Rajeev, Rehani; Rajamannar, Thennati; Patel,

S. Kartik; Arun, Yadav; Mukesh, Vaghela

PATENT ASSIGNEE(S):

Sun Pharmaceutical Ind. Ltd., India

SOURCE:

Indian, 13 pp. CODEN: INXXAP

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND DATE APPLICATION NO. DATE

PATENT NO. IN 186589 20011006 IN 1999-B0654 19990917

PRIORITY APPLN. INFO.:

IN 1999-B0654

19990917

OTHER SOURCE(S):

CASREACT 142:316575; MARPAT 142:316575

GI

A facile process is described for the preparation of iopamidol I, a non-ionic AB X-ray contrast medium. The process comprises of treatment of an aqueous solution

acetoxyiopamidol II [R = alkyl] with one or more of amine bases, and crystallization of iopamidol directly from the reaction mixture using alc. solvents

to furnish a pharmaceutically acceptable purified iopamidol. Thus, reacting L-5-α-acetoxypropionylamino-2,4,6-triiodoisophthalic acid di(1,3-dihydroxyisopropylamide) with MeNH2 in H2O for 5 h at room temperature followed by addition of 2-propanol and heating to 90°C until complete crystallization, afforded 67% iopamidol (US Pharmacopoeial grade).

L53 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN ACCESSION NUMBER: 2005:207867 CAPLUS

DOCUMENT NUMBER:

142:246293

TITLE:

A process for the preparation of substantially pure

APPLICATION NO.

DATE

gabapentin

INVENTOR(S):

Rajamannar, Thennati; Rajeev, Rehani Sun Pharmaceutical Industries Ltd., India

PATENT ASSIGNEE(S): SOURCE:

Indian, 16 pp. CODEN: INXXAP

DATE

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

KIND

PATENT INFORMATION:

PATENT NO.

	IN 188097	Α	20020817	IN 2000-MU62	20000120
	IN 191332	A	20031122	IN 2001-MU863	20010910
PRIC	RITY APPLN. INFO.:			IN 2000-MU62	A 20000120
AB	A process for the	preparat	ion of subst	cantially pure 1-(ami	nomethyl)-1-
				s described. The pro	
				entin with an alkali	
	of the reaction mi	xture is	at least 7	.5, heating the react	ion mixture to a
	temperature of at	least ab	out 80° and	maintaining said tem	perature for at least
				solvent followed by	
	substantially pure	gabaper	tin-lactam:	and (b) hydrolyzing	the
				with an acid to obtain	
				a base to precipitat	
				a base to precipitat	e gabapencin, and
	isolation of preci	priated	gapapentin.		

L53 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:1079731 CAPLUS

DOCUMENT NUMBER:

142:56160

TITLE:

process for purification of citalogram by

hydrogenolysis halogenated isobenzofuran impurities

INVENTOR(S):

Borase, Ashok Punju; Patel, Nileshkumar Sureshbai; Kilaru, Srinivasu; Thennati,

Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceuticals Industries Ltd., India

SOURCE:

Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 1486492	A2 20041215	EP 2004-291424	20040608
EP 1486492	A3 20050223		
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
IE, SI, LT,	LV, FI, RO, MK,	CY, AL, TR, BG, CZ,	EE, HU, PL, SK, HR
US 2005004380	A1 20050106	US 2004-865139	20040608
US 7019153	B2 20060328		
PRIORITY APPLN. INFO.:		IN 2003-MU602	A 20030610
OTHER SOURCE(S):	MARPAT 142:56160		
GI			

The present invention provides a process for decreasing the content of AB halogenated isobenzofuran impurities I (X = halo) in citalogram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalogram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

L53 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

2004:832438 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

141:297645

TITLE:

A process for the isolation of pure

1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition salt by neutralization

with base

INVENTOR(S):

Gurunath, Gaonkar Subhash; Rajamannar,

Thennati; Shrivastava, Ratnesh

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Ltd., India

SOURCE:

Indian, 10 pp. CODEN: INXXAP

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 186285	A	20010728	IN 2000-MU76	20000124
PRIORITY APPLN. INFO.:			IN 2000-MU76	20000124
AB A process is descri	bed for	the isolati	on of pure 1-	

(aminomethyl)cyclohexaneacetic acid (i.e., gabapentin) from an aqueous solution containing acid addition salt of 1-(aminomethyl)cyclohexaneacetic acid [e.g., 1-(aminomethyl)cyclohexaneacetic acid hydrochloride] by treatment with a base (e.g., sodium hydroxide) to the isoelec. point. The process yields pure 1-(aminomethyl)cyclohexaneacetic acid directly from the aqueous solution containing its acid addition salt, which salt is generated during the synthesis of 1-(aminomethyl)cyclohexaneacetic acid by the acid hydrolysis of its corresponding lactam.

L53 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:825284 CAPLUS

DOCUMENT NUMBER: 141:295724

TITLE: A process for the synthesis of 1-(2-nitroaryl)-2-

arylethanes and their substituted derivatives as key intermediates for the production of pharmaceutically

CODEN: INXXAP

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. APPLICATION NO. KIND DATE DATE -----_ _ _ _ _____ ------_ _ _ _ _ _ _ IN 182116 Α 19990102 IN 1996-B0362 19960712 PRIORITY APPLN. INFO.: IN 1996-B0362 19960712 GI

A process is described for the recovery of tramadol in the form of AB cis-tramadol hydrochloride, an analgesic drug I.HCl (no biol. data), from trans-tramadol hydrochloride II.HCl, or from a mixture of the diastereomeric cis- and trans-tramadols. The said process comprises isomerization of trans/cis, trans-tramadols under solvolytic conditions by catalysis with an appropriate acid resulting in enrichment of the cis-tramadol component which is then isolated as a pure isomer by crystallization This process when carried out in an iterative manner enables the recovery as cis-tramadol, in asymptotically quant. amts., from trans/cis, trans-tramadols.

NMe₂

II

L53 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:410231 CAPLUS

DOCUMENT NUMBER:

140:375168

TITLE:

A process for the preparation of 1-(2,3-epoxypropyl)-5nitroimidazoles via condensation of 5-nitroimidazoles

and epichlorohydrin

INVENTOR(S):

Rao, C. Trinadha; Rajamannar, T.; Acharyulu,

P. V. R.; Rehani, R.; Desouza, N. J.

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Ltd., India Indian, 26 pp.

SOURCE:

CODEN: INXXAP

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND	DATE	APPLICATION NO.	DATE
A	19980620	IN 1996-B0597	19961210
		IN 1996-BO597	19961210
			A 19980620 IN 1996-B0597

OTHER SOURCE(S):

CASREACT 140:375168; MARPAT 140:375168

GI

active compounds

INVENTOR(S): Rajamannar, T.; De Souza, N. J.

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India

SOURCE: 4 Indian, 27 pp.

CODEN: INXXAP

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

IN 181826 A 19981003 IN 1995-B0491 19951121

PRIORITY APPLN. INFO.: IN 1995-B0491 19951121

OTHER SOURCE(S): CASREACT 141:295724; MARPAT 141:295724

GI

$$R^3$$
 R^2 R^4 R^4 R^2

$$R^{1}$$
 $CO_{2}R$
 $CO_{2}R$
 R^{2}
 R^{2}
 R^{4}
 R^{4}
 R^{2}
 R^{2}

An ew process for the preparation of substituted 1,2-diarylethane derivs. I [X = H, halogens such as Cl, Br and I, and NO2; R1, R4 = H, usual aromatic substituent such as Cl, CH3, OCH3, CF3, NH2 and nitrogen heterocyclic residues; R2 = H, alkyl, (un)substituted aryl; R3 = H, CO2R (wherein R = H, alkyl)] which are key intermediates for the preparation of the well known tricyclic antidepressant drugs, such as clomipramine, imipramine, desipramine, lofepramine and trimipramine, is disclosed. The compds. I are produced by treating the compds. II [R1 is as defined above; R = alkyl] with compound III [R2, R4, X are as defined above; Y = a leaving group such as halo, OMs, OTs] followed by the work-up procedure. Twelve compds. I [R1 = 4-Cl; R2, R4 = H; R3 = CO2Me, CO2H, H] were prepared

L53 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:825283 CAPLUS

DOCUMENT NUMBER: 141:277348

TITLE: A process for the recovery of tramadol as cis-tramadol

hydrochloride in asymptotically quantitative amounts

from mixtures of diastereomers of tramadol

INVENTOR(S): Rajamannar, T.; Rao, Trinadha C.; Sebastian,

Sonny; De Souza, N. J.

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India

SOURCE: Indian, 22 pp.

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WO 2003057132
                                20040415
                          C1
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                          A1
                                20030724
                                            AU 2003-222435
                                                                    20030107
     AU 2003222435
                                20050224
                                                                   20040719 <--
     US 2005043550
                          A1
                                            US 2004-500532
                                            IN 2002-MU10
                                                                A 20020107
PRIORITY APPLN. INFO.:
                                            IN 2002-MU18
                                                                A 20020110
                                            IN 2002-MU847
                                                                A 20020930
                                            WO 2003-IN6
                                                                W 20030107
OTHER SOURCE(S):
                         CASREACT 139:117333; MARPAT 139:117333
```

GI

Title compound (I; R = cyano) (citalogram) was prepared by treatment AB of I (R = Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. PhMe layer was separated and the pH of the aqueous layer was adjusted to

with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and

0.23% of the amide and desmethylcitalopram resp.

L53 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

1

ACCESSION NUMBER:

2001:699013 CAPLUS

DOCUMENT NUMBER:

135:226785

TITLE:

Etherification and salification process for the industrial-scale manufacture of fluvoxamine maleate

INVENTOR(S):

Chitturi, Rao; Rajamannar, Thennati; Jadav, Kanaksinh Jesingbhai; Shah, Hemant Ashvinbhai

PATENT ASSIGNEE(S):

Sun Pharmaceutical Industries Ltd., India

$$\mathbb{R}^{1}$$
 \mathbb{R}^{2}
 \mathbb{R}^{3}
 \mathbb{R}^{3}

A process for the preparation of 1-(2,3-epoxypropyl)-5-nitroimidazoles I [R1, AB R2 = NO2, H, halo; R3 = H, halo, alkyl] via the regionelective N-alkylation of 5-nitroimidazoles II by epichlorohydrin in the presence of AlCl3 was provided. For example, to a suspension of 2-methyl-5nitroimidazole (250 g) in Et acetate (2.5 L) under N2 atmosphere was added dropwise anhydrous AlCl3 (328 g), while maintaining the reaction temperature between -10 to -5 $^{\circ}\text{C}$. Epichlorohydrin (273 g) was then added to the mixture over a 4-h period and the reaction stirred for addnl. 6-h at -10 to -5 °C. After aqueous work-up and treatment with NaOH, 1-(2,3-epoxypropyl)-2-methyl-5-nitroimidazole was obtained in 75% yield. Of note, the use of a Lewis acid instead of a base, as in the prior art, afforded exclusive formation of the 5-nitroimidazole derivative

L53 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:551309 CAPLUS

DOCUMENT NUMBER: 139:117333

TITLE: Process for the preparation of 1-[3-

(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-

5-isobenzofurancarbonitrile via cyanation of the

corresponding chloride or bromide precursors.

INVENTOR (S):

Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai,

Rajendran; Patel, Nileshkumar Sureshbhai

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

PCT Int. Appl., 41 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057132	A2	20030717	WO 2003-IN6	20030107
WO 2003057132	A3	20040226		

SOURCE: Patentschrift (Switz.), 6 pp.

CODEN: SWXXAS

DOCUMENT TYPE:

Patent German

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
CH 691124	A	20010430	CH 2000-2194		20001111
IN 186677	А	20011020	IN 1999-B0796		19991112
US 6433225	B1	20020813	US 2000-696613		20001025
IT 1319242	B1	20030926	IT 2000-MI2324		20001026
BE 1012819	A6	20010306	BE 2000-717		20001110
PRIORITY APPLN.	INFO.:		IN 1999-B0796	A	19991112

OTHER SOURCE(S): CASREACT 135:226785

Fluvoxamine maleate is prepared on an industrial scale by the etherification 5-methoxy-4'-trifluoromethylvalerophenone oxime with 2-chloroethylamine hydrochloride in the presence of bases (e.g., potassium hydroxide) and polyether catalysts (e.g., polyethylene glycol) yielding fluvoxamine which is then salified with maleic acid.

=> d que 145

L1 1 SEA FILE=CAPLUS ABB=ON PLU=ON US2004-500532/AP L19

Structure attributes must be viewed using STN Express query preparation.

L21 385 SEA FILE=REGISTRY SSS FUL L19

L36 STR

Structure attributes must be viewed using STN Express query preparation. L37 STR

Structure attributes must be viewed using STN Express query preparation.

49	SEA	FILE=REGISTF	RY SUB=L2	21 SSS FU	JL L36	
180	SEA	FILE=REGIST	RY SUB=L2	21 SSS FU	JL L37	
115	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L41 (L)	PREP+ALL/RL
26	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L39 (L)	RACT+ALL/RL
25	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	L42 AND	L43
25	SEA	FILE=CAPLUS	ABB=ON	PLU=ON	(L44 OR	L1)
	180 115 26 25	180 SEA 115 SEA 26 SEA 25 SEA	180 SEA FILE=REGISTF 115 SEA FILE=CAPLUS 26 SEA FILE=CAPLUS 25 SEA FILE=CAPLUS	180 SEA FILE=REGISTRY SUB=L2 115 SEA FILE=CAPLUS ABB=ON 26 SEA FILE=CAPLUS ABB=ON 25 SEA FILE=CAPLUS ABB=ON	180 SEA FILE=REGISTRY SUB=L21 SSS FU 115 SEA FILE=CAPLUS ABB=ON PLU=ON 26 SEA FILE=CAPLUS ABB=ON PLU=ON 25 SEA FILE=CAPLUS ABB=ON PLU=ON	49 SEA FILE=REGISTRY SUB=L21 SSS FUL L36 180 SEA FILE=REGISTRY SUB=L21 SSS FUL L37 115 SEA FILE=CAPLUS ABB=ON PLU=ON L41 (L) 26 SEA FILE=CAPLUS ABB=ON PLU=ON L39 (L) 25 SEA FILE=CAPLUS ABB=ON PLU=ON L42 AND 25 SEA FILE=CAPLUS ABB=ON PLU=ON (L44 OR

=> d ibib abs hitstr 145 tot

L45 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2006:213262 CAPLUS

DOCUMENT NUMBER:

144:292567

TITLE:

Process for preparation of escitalopram

INVENTOR(S):

Pulla Reddy, Muddasani; Sambasiva Rao, Talasila;

Venkaiah Chowdary, Nannapaneni

PATENT ASSIGNEE(S):

Natco Pharma Limited, India

SOURCE:

PCT Int. Appl., 22 pp. CODEN: PIXXD2

C

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND				D	DATE APPLICATION NO.						DATE						
					-												
WO	2006	0250	71		A1		2006	0309	1	WO 2	005-	IN28:	2		2	0050	823 [°]
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KM,	KP,	KR,	ΚZ,
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,
		NG,	NI,	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,
		SL,	SM,	SY,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,
		ZA,	ZM,	ZW													
	RW:	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
		IS,	IT,	LT,	LU,	LV,	MC,	ΝL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,
		CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,
		GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚŻ,	MD,	RU,	TJ,	TM										

PRIORITY APPLN. INFO.:

IN 2004-CH885 A 20040902

The present invention relates to an improved process for the preparation of escitalopram which consists of a sequential double Grignard reaction on 5-iodophthalide to get the dihydroxy compound, its resolution using a chiral acid, cyclization of resolved compound, and cyanation of compound using DMF and CuCN. The present process utilizes the facile displacement of iodo group with cyano group in the final step of the preparation of escitalopram. Escitalopram is a widely used anti-depressant.

IT 878655-30-2P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (intermediate; preparation of escitalopram)

RN 878655-30-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 128196-01-0P, Escitalopram 219861-08-2P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of escitalopram)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2005:472143 CAPLUS

DOCUMENT NUMBER:

143:26491

TITLE:

A process for the preparation of high purity

escitalopram

CM 2

CRN 7601-90-3 CMF Cl H O4

IT 59729-33-8P, Citalopram 219861-08-2P, Escitalopram
 oxalate

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of high purity escitalopram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 219861-08-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

RN 852705-14-7 CAPLUS

CN Methanesulfonic acid, trifluoro-, compd. with (1S)-5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-1-isobenzofuranpropanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 1493-13-6 CMF C H F3 O3 S

RN 852705-15-8 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, perchlorate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 852705-13-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, methanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 75-75-2 CMF C H4 O3 S

CM 2

CRN 64-19-7 CMF C2 H4 O2

RN 852705-11-4 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, benzoate (9CI) (CA INDEX NAME)

CM 1

CRN 488148-14-7 CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 65-85-0 CMF C7 H6 O2

RN 852705-12-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 852705-10-3 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)-, acetate (9CI) (CA INDEX NAME)

CM 3

CRN 488148-14-7

CMF C19 H21 Br F N O

Absolute stereochemistry. Rotation (+).

INVENTOR(S): Pullareddy, Muddasani; Sambasiva Rao, Talasila;

Srinivasa Rao, Nekkanti; Venkaiah Chowdary,

Nannapaneni

PATENT ASSIGNEE(S): Natco Pharma Limited, India

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: Engli

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.			KIN	D	DATE		APPLICATION NO.					DATE						
						-												
WO	WO 2005049596		A1	A1 20050€			2 WO 2003-IN363						20031120					
	W :	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	GE,	
		GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KZ,	LC,	LK,	
		LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	
		OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	
		TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw			
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	
		BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	
		TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG
AU 2003282383			A1		2005	0608	AU 2003-282383				20031120							
PRIORITY APPLN. INFO.:							1	WO 2	003-	IN363	3	7	A 20	0031	120			
OTHER SC	URCE	(S):			CAS	REAC	T 14	3:264	191									
GI																		

The present invention discloses an improved process for the preparation of high purity escitalopram base (I, R = CN) by reacting the acid addition salt of I (R = Br) with copper(I) cyanide and with or without copper(I) iodide in DMF medium at 145-150 °C. Cyanation of the acid addition salt is superior in yield and quality over the parent base compound I (R = Br). The process is compatible to scale up operations thereby making the process com. viable for escitalopram oxalate. Escitalopram oxalate is an antidepressant available in the market.

Ι

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

IT 64169-39-7

RL: RCT (Reactant); REM (Removal or disposal); PROC (Process);
RACT (Reactant or reagent)

(process for purification of citalopram by hydrogenolysis halogenated impurities)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:691476 CAPLUS

DOCUMENT NUMBER: 141:207048

TITLE: Preparation of pure citalogram

INVENTOR(S): Kaushik, Vipin Kumar; Rao, Divvela Venkata Naga

Srinivasa; Handa, Vijay Kumar; Sivakumaran,

Meenakshisunderam

PATENT ASSIGNEE(S): Aurobindo Pharma Ltd., India

SOURCE: U.S., 3 pp. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6781003	B1	20040824	US 2003-456135	20030609
PRIORITY APPLN. INFO.:			US 2003-456135	20030609

OTHER SOURCE(S): CASREACT 141:207048

GI

The present invention relates to an industrially advantageous method for the purification of citalopram (I) wherein desmethyl citalopram (II), present in crude citalopram as an impurity, is methylated to produce pure citalopram I. The resulting citalopram product I is isolated as the base or a pharmaceutically acceptable salt thereof. Thus, to crude citalopram (90 g, 0.28 mol) containing desmethyl citalopram (7 %, HPLC), formic acid (98%, 2.7 g) was added followed by aqueous formaldehyde(35%, 2.37 g). The reaction mass was heated at 85-95° for 30 min, cooled to 30°, and diluted with ethanol (900 mL), treated with oxalic acid dihydrate (41.94 g, 0.33 mol), and heated to reflux. The obtained solution was cooled to 20-25° and stirring was continued for 2 h at 20-25°, followed by collecting the product by filtration and recrystn. from ethanol to give highly pure 92 g crystalline citalopram oxalate having HPLC purity 99.7% wherein desmethyl citalopram (impurity) was not detected.

IT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(preparation of pure citalopram by N-methylation of crude citalopram containing

desmethyl citalogram with formaldehyde and formic acid)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

US 7019153

B2 20060328

PRIORITY APPLN. INFO.:

IN 2003-MU602

A 20030610

OTHER SOURCE(S):

MARPAT 142:56160

GI

AB The present invention provides a process for decreasing the content of halogenated isobenzofuran impurities I (X = halo) in citalopram (II) by hydrogenolysis to I (X = H). Thus, 5 g crude citalopram base containing 4.84% of bromo impurity I (X = Br) is dissolved in 50 mL EtOAc, 0.1 g Pd/C and 0.1 g sodium hypophosphite added and the mixture refluxed for 2 h. Anal. showed that the bromo impurity I (X = Br) is absent.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Citalopram 207559-01-1P, Citalopram oxalate

RL: PUR (Purification or recovery); PREP (Preparation)
(process for purification of citalogram by hydrogenolysis halogenated impurities)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$^{\text{NC}}$$
 $^{\text{O}}$ $^{\text{CH}_2)}_3$ $^{\text{NMe}_2}$

• HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RL: RCT (Reactant); RACT (Reactant or reagent)

(process for purification of citalogram via washing with polybasic acid solns.)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

IT 128196-01-0P, Escitalopram

RL: SPN (Synthetic preparation); PREP (Preparation)

(process for purification of citalogram via washing with polybasic acid solns.)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

L45 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:1079731 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

142:56160

TITLE:

process for purification of citalogram by

hydrogenolysis halogenated isobenzofuran impurities Borase, Ashok Punju; Patel, Nileshkumar Sureshbai;

Kilaru, Srinivasu; Thennati, Rajamannar

PATENT ASSIGNEE(S):

Sun Pharmaceuticals Industries Ltd., India

SOURCE:

Eur. Pat. Appl., 17 pp. CODEN: EPXXDW

CODEN:

DOCUMENT TYPE:

Patent English

LANGUAGE:

Fudits

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE		
EP 1486492	A2 20041215	EP 2004-291424	20040608		
EP 1486492	A3 20050223				
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IT, LI, LU, NL,	SE, MC, PT,		
IE, SI, LT,	LV, FI, RO, MK,	CY, AL, TR, BG, CZ, EE,	HU, PL, SK, HR		
US 2005004380	A1 20050106	US 2004-865139	20040608		

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

1

ACCESSION NUMBER:

PATENT ASSIGNEE (S):

2005:120910 CAPLUS

DOCUMENT NUMBER:

142:197860

TITLE:

Process for purification of citalogram via washing

with polybasic acid solutions

INVENTOR(S):

Uttarwar, Sunil Govindrao; Gawli, Bhagwan Narayan

Meditab Specialities Pvt. Ltd., India; Wain,

Christopher Paul

SOURCE:

PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATEN	PATENT NO.				KIND DATE			APPLICATION NO.						DATE			
	050122			A2 A3		2005		Ţ	WO 2	004-0	GB32	09		20	0040	723	
	: AE, CN,	AG, CO,	AL, CR,	AM, CU,	AT, CZ,	AU, DE, ID,	AZ, DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
	LK, NO,	LR, NZ,	LS, OM,	LT, PG,	LU, PH,	LV, PL, TZ,	MA, PT,	MD, RO,	MG, RU,	MK, SC,	MN, SD,	MW, SE,	MX, SG,	MZ, SK,	NA, SL,	NI, SY,	
R	W: BW, AZ, EE,	GH, BY, ES,	GM, KG, FI,	KE, KZ, FR,	LS, MD, GB,	MW, RU, GR,	MZ, TJ, HU,	NA, TM, IE,	SD, AT, IT,	SL, BE, LU,	SZ, BG, MC,	TZ, CH, NL,	UG, CY, PL,	ZM, CZ, PT,	ZW, DE, RO,	AM, DK, SE,	
CP 24	SN,	TD,	TG	BF,	•	CF,		-	•	•	GN, 1023	~.	GW,	·	•	•	
GB 2418916 PRIORITY APPLN. INFO.:			AI		2006	U412	(GB 2	003-	1023 1747! GB32!	5	_	A 2	0040' 0030' 0040'	725		

OTHER SOURCE(S): CASREACT 142:197860

AB A process for purification of racemic or optically active citalopram (I) comprises (i) providing crude I containing ≥1 I derivs. dissolved in a H2O-immiscible organic solvent, (ii) washing the crude mixture with ≥1 dilute aqueous solution of a polybasic acid, either in free form or as a partial

alkali metal salt, so as to sep. I from impurities present in the crude mixture; and (iii) where required converting purified I free base to a pharmaceutically acceptable salt. Thus, 4-[4-(dimethylamino)-1-(4'-fluorophenyl)-1-hydroxybutyl]-3-hydroxymethylbenzonitrile was heated at 105° in aqueous H3PO4 followed by cooling, dilution with H2O, pH adjustment to 8-10 with aqueous NH3, and extraction with EtOAc. The EtOAc

layer

was washed with aqueous disodium edetate followed by drying over Na2SO4, treatment with decolorizing C, and filtration to give >99.85% pure citalopram hydrobromide.

IT 59729-33-8P, Citalopram

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (process for purification of citalogram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 59729-32-7P, Citalopram hydrobromide

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (process for purification of citalogram via washing with polybasic acid solns.)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$^{\text{NC}}$$
 $^{\text{O}}$ $^{\text{CH}_2)}$ 3 $^{\text{NMe}_2}$

• HBr

IT 64169-39-7

A processes for preparation of escitalopram, useful as TITLE:

antidepressant

INVENTOR(S): Nannapaneni, Venkaiah Chowdary; Muddasani, Pulla

Reddy; Talasila, Sambashiva Rao; Nekkanti, Srinivasa

Rao; Podile, Khadgapathi

Natco Pharma Limited, India PATENT ASSIGNEE(S):

PCT Int. Appl., 30 pp. SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.					KIND DATE			APPLICATION NO.						DATE			
	WO 20	0040	0653	75		A1	-	2004	0805	1	WO 2	003-	IN22	0		2	0030	617
	7	W :	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
	GM, HR, HU			HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	
	LS, LT, LU			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NI,	NO,	NZ,	OM,	
	PH, PL, PT			PT,	RO,	RU,	SC,	SD;	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	
			TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW					
	1	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
			KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
			FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
	BF, BJ, CF,			CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
	AU 2003242990			A1 20040813			3 AU 2003-242990					20030617						
PRIO	PRIORITY APPLN. INFO.:								IN 2003-MA52					A 20030117				
									1	WO 2	003-	IN22	0	1	W 2	0030	617	

OTHER SOURCE(S):

CASREACT 141:157024

The present invention relates to an improved process for the preparation of AB escitalopram (I) which consist of a sequential double Grignard reaction on 5-bromophthalide, isolation of di-magnesium salt, neutralization of di-magnesium salt, resolution of dihydroxy compound of the formula II, cyclization, and cyanation. The proposed process utilizes the insol. property of di-magnesium salt in a mixture of THF and a non-polar organic solvent, and separates it from impurities by simple filtration thereby making the isolation and purification process simple. Advantages of the proposed process include (a) high yield preparation of escitalopram (>25%), (b) escitalopram can be prepared in a simple and easy to adopt manner without involving any purification steps, (c) the process produces pure (>98%)

IT 59729-32-7P, Citalopram Hydrobromide

RL: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)

(preparation of pure citalopram by N-methylation of crude citalopram containing

desmethyl citalopram with formaldehyde and formic acid)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

NC
$$O$$
 (CH₂)₃-NMe₂

• HBr

IT **64169-39-7**, 5-Bromo-1-(3-dimethylaminopropyl)-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of pure citalopram by N-methylation of crude
citalopram containing desmethyl citalopram with formaldehyde and formic
acid)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2004:633919 CAPLUS

DOCUMENT NUMBER:

141:157024

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:331827 CAPLUS

DOCUMENT NUMBER: 140:357194

TITLE: Process for the manufacture of citalogram hydrobromide

from 5-bromophthalide

INVENTOR(S): Chodankar, Nandkumar; Bhobe, Ajit; Oak, G. M.; Eappan,

Philip

PATENT ASSIGNEE(S): Sekhsaria Chemicals Limited, India

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004077870	A1	20040422	US 2002-277451	20021022
US 6812355	B2	20041102		
PRIORITY APPLN. INFO.:			US 2002-277451	20021022
OTHER SOURCE(S):	CASRE	ACT 140:3571	94; MARPAT 140:357194	

Disclosed is a process for the preparation of 1-(4-fluorophenyl)-1-(3-dimethylamino-propyl)-5-phthalanecarbonitrile (citalopram) (known antidepressant) or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide using p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium chloride, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields.

IT 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylaminopropyl)-5-bromophthalane

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(manufacture of citalopram hydrobromide from 5-bromophthalide by two successive Grignard reactions on 5-bromophthalide using

p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium chloride)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P
207559-01-1P, Citalopram oxalate 500733-84-6P,

Citalopram acetate

RL: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)

(manufacture of citalopram hydrobromide from 5-bromophthalide by two successive Grignard reactions on 5-bromophthalide using

di-magnesium salt of intermediate compound was isolated, etc.

IT 128196-01-0P, Escitalopram 128196-02-1P,

R-(-)-Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic

preparation); PREP (Preparation)

(processes for the preparation of escitalopram and its precursor)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-

fluorophenyl) -1,3-dihydro-, (1S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 128196-02-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

IT 488148-14-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(processes for the preparation of escitalopram and its precursor)

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

p-fluorobromobenzene and then N,N-dimethylaminopropylmagnesium
chloride)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$^{\text{NC}}$$
 $^{\text{O}}$ $^{\text{CH}_2)_3-\text{NMe}_2}$

• HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 500733-84-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 64-19-7 CMF C2 H4 O2

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:101152 CAPLUS

DOCUMENT NUMBER: 140:145992

TITLE: Process for the preparation of 1-(3-

dimethylaminopropyl) -1-(4-fluorophenyl)
-1,3-dihydroisobenzofuran-5-carbonitrile

INVENTOR(S): Hilden, Leif; Rummakko, Petteri; Grumann, Arne;

Pietikaeinen, Pekka

PATENT ASSIGNEE(S): Orion Corporation Fermion, Finland

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE			
WO 2004011450	A1	20040205	WO 2003-FI557	20030710			
W: AE, AG,	AL, AM, AT	r, AU, AZ, 1	BA, BB, BG, BR, BY, BZ	, CA, CH, CN,			
CO, CR,	CU, CZ, DE	E, DK, DM,	DZ, EC, EE, ES, FI, GB	, GD, GE, GH,			
GM, HR,	HU, ID, IL	, IN, IS,	JP, KE, KG, KP, KR, KZ	, LC, LK, LR,			

REFERENCE COUNT:

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:837069 CAPLUS

DOCUMENT NUMBER:

139:337880

TITLE:

Preparation of escitalopram via the chiral enriched diol monoesters of (4-bromo-2-(hydroxymethyl)phenyl)-

(4-fluorophenyl) methanol

INVENTOR(S):

Tse, Hoi Lun Allan

PATENT ASSIGNEE(S): SOURCE:

Torcan Chemical Ltd., Can. PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		APPLICATION NO.				
WO 2003087081	A1 20031023	WO 2003-CA522	20030408			
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY,	BZ, CA, CH, CN,			
CO. CR. CU.	CZ, DE, DK, DM,	DZ, EC, EE, ES, FI,	GB, GD, GE, GH,			
		JP, KE, KG, KP, KR,				
		MK, MN, MW, MX, MZ,				
		SE, SG, SK, SL, TJ,				
	US, UZ, VC, VN,		111, 111, 111, 111,			
			714 AM A7 DV			
		SL, SZ, TZ, UG, ZM,				
		BE, BG, CH, CY, CZ,				
		LU, MC, NL, PT, RO,				
BF, BJ, CF,	CG, CI, CM, GA,	GN, GQ, GW, ML, MR,	NE, SN, TD, TG			
CA 2381341	AA 20031009	CA 2002-2381341	20020409			
AU 2003218575	A1 20031027	AU 2003-218575	20030408			
		EP 2003-711761				
		GB, GR, IT, LI, LU,				
		CY, AL, TR, BG, CZ,				
		US 2005-510890				
		CA 2002-2381341				
INIONIII AIIIN. INIO		WO 2003-CA522				
OTHER SOURCE(S):	CASREACT 139:33		= 3 - 2 - 2 - 3			

GI

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003244676 20040216 AU 2003-244676 Α1 20030710 US 2005209467 20050922 **A1** US 2005-45087 20050131 PRIORITY APPLN. INFO.: FI 2002-1421 20020730 US 2002-419150P Ρ 20021018 WO 2003-FI557 W 20030710 OTHER SOURCE(S): CASREACT 140:145992; MARPAT 140:145992

GI

AB The present invention is directed to novel processes for the preparation of citalopram comprising halogenation of a phthalides I (wherein R is a suitable group to be changed to CN) to afford an acid halides II (X is halogen) and thereafter obtaining citalogram through two successive reactions with suitable organometallic halides or organoboranes or by a reaction with organometallic 4-fluorophenylhalide or 4-fluorophenylborane followed by reduction and alkylation, and an exchange of R to cyano to afford citalopram. The order of the reactions can be varied depending e.g. on the starting compound used.

59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of citalogram)

RN59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-(CA INDEX NAME) fluorophenyl) -1,3-dihydro- (9CI)

ΤТ 64169-45-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of citalogram)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 219861-08-2 CAPLUS

5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-CNfluorophenyl)-1,3-dihydro-, (1S)-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 128196-01-0 CMF C20 H21 F N2 O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:590880 CAPLUS

DOCUMENT NUMBER:

139:133459

TITLE:

Cyanation process for the preparation of citalogram

and its extractive purification

INVENTOR(S):

Coppi, Laura; Gasanz Guillen, Yolanda; Campon Pardo,

Julio

PATENT ASSIGNEE(S):

Esteve Quimica, S.A., Spain

SOURCE:

U.S. Pat. Appl. Publ., 5 pp.

NC
$$\begin{array}{c} \text{Br} & \text{CH}_2\text{-O-COCH}_3 \\ \text{OH} & \text{OH} \\ \text{CH}_2\text{-CH}_2\text{-CH}_2\text{-NMe}_2 \\ \text{F} & \text{II} \end{array}$$

AB Preparation of escitalopram (I) via the chiral enriched monoacetate ester of (4-bromo-2-(hydroxymethyl)phenyl)-(4-fluorophenyl)methanol (II) was disclosed. For example, a racemic mixture of monoacetate ester II (13.52 g) and (+)-di-p-toluoyl tartaric acid (11.92 g) in acetone (135 mL) was heated at reflux until a pale brown solution was obtained. The solution was cooled, the acetone removed under vacuum and the resulting brown foam recrystd. from acetone-hexane (2:1) to afford the (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II with a diastereomeric ratio of 97:3. Of note, the claimed (+)-di-p-toluoyl tartaric acid salt of monoacetate ester II was converted to escitalopram oxalate in 4-steps with [α]D = +10.1° (at 20°C, c 0.95 in MeOH).

IT 488148-14-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of escitalopram via a chiral enriched diol monoester intermediate)

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)~ (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

IT 128196-01-0P, Escitalopram 219861-08-2P, Escitalopram oxalate

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of escitalopram via a chiral enriched diol monoester intermediate)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE:

NTT. 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO. KIND DA				DATE				LICAT	NO.	•	D						
		2003						2003			US	2003-	3512	89		2	0030	124
	-	6635				B2		2003										
		2194						2003			ES	2002-	167			2	0020	125
		2194				В2		2004										
		2474										2003-					0030	124
	WO	2003										2003-					0030	
		W:										, BG,						
			CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	, EE,	ES,	FI,	GB,	GD,	GE,	GH,
			GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,
			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
												SL,						
			UA,	UG,	US,	UΖ,	VC,	VN,	ΥU,	ZA,	z_{M}	, ZW						-
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ	, TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
												, CH,						
												, NL,						
												, ML,						•
	ΕP	1479										2003-						124
												, IT,						
												, TR,						,
	JP	2005										2003-						124
												2003-						
												2004-						
												2004-					0040	
PRIO		APP										2002-					0020	
												2003-			į		0020	
7.70	a														•	. –		

AB Crude citalopram was prepared the cyanation of 1-[3-(dimethylamine)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-bromoisobenzofuran with copper cyanide and purified citalopram or one of its salts (e.g., citalopram hydrobromide) was obtained by the extractive purification of citalopram by selective extns. of citalopram or it salts of its impurities with organic solvents (e.g., toluene and heptane) and water under specific conditions of pH and temperature TT 59729-33-8P, Citalopram

RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyanation process for the preparation of citalopram and its extractive purification) $\label{eq:cyanation}$

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)

(cyanation process for the preparation of citalogram and its extractive purification)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

Br O F Me₂N- (CH₂)₃

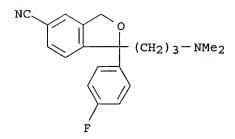
IT 59729-32-7P, Citalopram hydrobromide

RL: SPN (Synthetic preparation); PREP (Preparation)

(cyanation process for the preparation of citalogram and its extractive purification)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)



• HBr

L45 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:551309 CAPLUS

DOCUMENT NUMBER: 139:117333

TITLE: Process for the preparation of 1-[3-

(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-

5-isobenzofurancarbonitrile via cyanation of the

corresponding chloride or bromide precursors.

INVENTOR(S): Thennati, Rajamannar; Kilaru, Srinivasu; Chinnapillai,

Rajendran; Patel, Nileshkumar Sureshbhai

Rajendran; Patel, Nileshkumar Sureshbhai

PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2003-IN6
                                                                   20030107
    WO 2003057132
                          A2
                                20030717
    WO 2003057132
                          Α3
                                20040226
    WO 2003057132
                          Cl
                                20040415
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20030724
                                           AU 2003-222435
    AU 2003222435
                          A1
                                            US 2004-500532
    US 2005043550
                          A1
                                20050224
                                                                   20040719 <--
PRIORITY APPLN. INFO.:
                                            IN 2002-MU10
                                                                A 20020107
                                            IN 2002-MU18
                                                                Α
                                                                   20020110
                                            IN 2002-MU847
                                                                Α
                                                                   20020930
                                            WO 2003-IN6
                                                                   20030107
                         CASREACT 139:117333; MARPAT 139:117333
OTHER SOURCE(S):
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GT

Title compound (I; R = cyano) (citalogram) was prepared by treatment of I (R = cyano) AB Cl, Br) with a cyanide source in the presence of I- in an amide, amine, or polyether solvent followed by treatment of the crude product containing 1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5isobenzofurancarbonitrile and 5-carboxamido-1-(3-dimethylaminopropyl)-1-(4fluorophenyl)phthalide impurities with a phosphorus oxyhalide, phosphorus oxide cyanide reversal agent, and purification using a solvent system comprising a hydrocarbon and alc., ester, ether, ketone, or mixture thereof. Thus, citalopram containing 4.7% amide and 0.72% desmethylcitalopram impurities was heated with POCl3 in PhMe at 70° for 1 h. The mixture was poured into water and pH was adjusted to 2.0-2.5 with aqueous HCl. PhMe layer was separated and the pH of the aqueous layer was adjusted to 9.0-9.5

with aqueous NH3 followed by extraction with PhMe to give product containing 0.05% and

0.23% of the amide and desmethylcitalopram resp.

59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Ι

1-[3-(Dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5isobenzofurancarbonitrile

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of citalogram via cyanation of the corresponding chloride or bromide precursor)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$NC$$
 O $(CH2)3-NMe2$

HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of citalogram via cyanation of the corresponding chloride or bromide precursor)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

Br
$$Me_2N-(CH_2)_3$$

L45 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:282554

DOCUMENT NUMBER:

138:305791

TITLE:

Process for the preparation of citalogram, and

intermediates and derivatives

CAPLUS

INVENTOR(S):

Malik, A. Aslam; Palandoken, Hasan; Stringer, Joy A.; Huang, Dershing; Romero, Antonio; Dapremont, Olivier

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L45 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

2001:31487 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 134:102526

Process for the synthesis of citalogram TITLE:

Bolzonella, Eva; Castellin, Andrea; Nicole, Andrea Vis Farmaceutici S.p.A., Italy INVENTOR(S):

PATENT ASSIGNEE(S):

PCT Int. Appl., 21 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.					KIND DATE			APPLICATION NO.						DATE			
	WO	2001				A2		2001			WO 2	000-	EP64:	 26			0000	706
	WO	2001	0023	83		А3		2001	0503									
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	ΒY,	ΒZ,	CA,	CH,	CN,
			CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,
			HU,	ID,	ΙL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,
			LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,
			SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,
			YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM				
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	AT,	BE,	CH,	CY,
			DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
			CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
	IT	99MI	1486			A1		20010108 IT 1999-MI1486							1	9990	706	
					AA		2002	0117		CA 2	001-	2383	963		2	0010	706	
	WO 2002004435				A1		2002	0117		WO 2	001-	DK48	1		2	0010	706	
		W:					ΑT,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EE,	EE,	ES,	FI,
			FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,
			KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,
			MZ,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SK,	SL,	TJ,	TM,
			TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	KZ,
			MD,	RU,	TJ,	TM												
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	AT,	BE,	CH,	CY,
								GB,										
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
	BR	2001	0069	76		A		2002	0723		BR 2	001-	6976			2	0010	706
	NO 2002001118				A		2002	0424		NO 2	002-	1118			2	0020	306	
	US 2002128497			A1		2002	0912		US 2	002-	9614	9		2	0020	306		
PRIO	RIT	Y APP	LN.	INFO	. :					IT 1999-MI1486						A 19990706		706
	OKIII MILIN. IMO							WO 2000-EP6426					A 20000706					
	•							WO 2001-DK481					W 20010706					
7 17				:		1		£	-1-		h i			-1		-b		

AB A new process is described for the synthesis of citalogram characterized by the conversion of 1-(4'-fluorophenyl)1-3-(dimethylaminopropyl)-5-

AB A method for the preparation of citalopram is presented, comprising the reaction of isobenzofuranpropanamine I, wherein R is Cl or Br, with a cyanide source in the presence of a nickel catalyst and isolation of the corresponding 5-cyano compound, i.e. citalopram.

I

IT 64169-39-7, 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)1,3-dihydro-N,N-dimethyl- 64169-45-5, 1Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl-

RL: RCT (Reactant); RACT (Reactant or reagent)
(method for the preparation of citalogram by nickel-catalyzed cyanation of halo precursors)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

IT 59729-33-8P, Citalopram

RL: SPN (Synthetic preparation); PREP (Preparation)
(method for the preparation of citalogram by nickel-catalyzed cyanation of halo precursors)

RN 59729-33-8 CAPLUS

Saloni Sharma

CH 2001-545

A 20010322

OTHER SOURCE(S):

CASREACT 135:61224; MARPAT 135:61224

AB A process for the preparation and purification of citalogram (I) is presented in

which a benzoisofuran derivative [II; Z = iodo, bromo, chloro, CF3(CF2)nS020; n = 0-8] is subjected to a cyanide-exchange reaction with a cyanide source (e.g., cuprous cyanide). The resultant crude citalopram is optionally subjected to some initial purification and subsequently treated with an amide or an amide-like group forming agent (e.g., acetic anhydride), the reaction mixture is then subjected to an acid/base wash and/or crystallization

and

recrystn. of citalopram in order to remove the amides formed from the crude citalopram mixture, and the resulting citalopram product is optionally further purified, worked up and isolated as the base or a pharmaceutically acceptable salt.

IT 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

Ι

(method for the preparation and purification of citalogram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7 64169-45-5 260066-78-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(method for the preparation of citalogram by the cyanidation of)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 260066-78-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:386023 CAPLUS

DOCUMENT NUMBER:

134:353251

TITLE:

Method for the preparation of citalogram by

nickel-catalyzed cyanation of halo precursors

INVENTOR(S):

Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S):

H Lundbeck A/S, Den.

SOURCE:

Brit. UK Pat. Appl., 16 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				- -
GB 2354240 A1		20010321	GB 2001-1508	19991119
PRIORITY APPLN. IN	FO.:		DK 1999-921 ·	19990625
			WO 1999-DK643	19991119

OTHER SOURCE(S):

MARPAT 134:353251

260066-78-2 CAPLUS RN

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,Ndimethyl- (9CI) (CA INDEX NAME)

IT 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of high-purity citalopram by cyanidation with purification via thin-film distillation)

RN59729-33-8 CAPLUS

5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-CN fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

CAPLUS COPYRIGHT 2006 ACS on STN L45 ANSWER 21 OF 25

ACCESSION NUMBER: 2001:472398 CAPLUS

DOCUMENT NUMBER: 135:61224

TITLE: Method for the preparation and purification of

citalopram

INVENTOR(S): Villa, Marcos; Sbrogio, Federico; Dancer, Robert

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den. SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.					KIND DATE			APPLICATION NO.							DATE				
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1	WO 2001045483 A						;	2001	0628		WO 2001-DK147						20010307			
1	WO 2001045483					A3 20011			20011227											
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             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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     EP 1181713
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     EP 1462447
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     AT 277920
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     ES 2228824
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                                  20020422 DK 2001-402
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                                  20010704 GB 2001-5983
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                                             CH 2001-1411
ES 2001-1762
AU 2001-65477
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    ES 2170732 A1
AU 744112 B1
SE 2001003045 A
SE 517623 C2
BG 106203 A
ZA 2001010179 A
NZ 516298 A
HR 2002000004 A1
US 2002120005 A1
US 6455710 B2
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                                             NZ 2001-516298
                                  20021220
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                           A1
A1
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                                                                         20020104
                                  20020829
                                               US 2002-46126
                                                                         20020108
                                  20020924
                                               DK 2000-1929 A 20001222
NL 2001-1017525 A 20001222
EP 2001-913726 A3 20010307
WO 2001-DK147 W 20010307
PRIORITY APPLN. INFO.:
                                                GB 2001-5983
                                                                     A3 20010312
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Saloni Sharma 06/19/2006

TD 1101070	D 1	20020020		
EP 1181272	B1		O OD TO II III W	OF MO DE
			B, GR, IT, LI, LU, NL,	SE, MC, PI,
IE, SI, LT,			DD 2001 (271	20010207
BR 2001006271	A	20020521	BR 2001-6271	20010307
TR 200200018	T1	20020621	TR 2002-18	20010307
AT 222899	E	20020915	AT 2001-913727	20010307
PT 1181272	T	20030131	PT 2001-913727	20010307
ES 2181663	T3	20030301	ES 2001-1913727	20010307
JP 2003519121	T2	20030617	JP 2001-549350	20010307
SK 284418	B6	20050401	SK 2001-1847	20010307
NL 1017534	C1	20010426	NL 2001-1017534	20010308
DK 200100386	A5	20020629	DK 2001-386	20010308
IN 193426	A	20040717	IN 2001-MA215	20010309
GB 2356199	A1	20010516	GB 2001-5981	20010312
GB 2356199	B2	20011003		
CZ 293140	B6	20040218	CZ 2001-891	20010312
FI 108640	B1	20020228	FI 2001-501	20010313
NO 2001001272	A	20020701	NO 2001-1272	20010313
NO 313047	В1	20020805		
GR 2001100131	A	20021009	GR 2001-100131	20010316
DE 10112828	C1	20021121	DE 2001-10112828	20010316
DE 10164725	A1	20030206	DE 2001-10164725	20010316
DE 10164725	B4	20040826		
CH 691536	A	20010815	CH 2001-546	20010322
BE 1013417	A6	20011204	BE 2001-189	20010322
FR 2818977	A1	20020705	FR 2001-4025 .	20010326
FR 2818977	В1	*		
NL 1018410	C1	20011113	NL 2001-1018410	20010628
BE 1013316	A6	20011106	BE 2001-466	20010709
GB 2361697	A1	20011031	GB 2001-17095	20010713
IN 193611	Α	20040724	IN 2001-MA580	20010713
CH 691999	Α	20010726	CH 2001-1412	20010726
ES 2170733	A1	20020801	ES 2001-1763	20010727
ES 2170733	В1	20031216		
AU 750006	В1	20020711	AU 2001-65478	20010827
SE 2001003044	Α	20020629	SE 2001-3044	20010914
ZA 2001010133	Α	20030113	ZA 2001-10133	20011210
BG 106219	Α	20020830	BG 2001-106219	20011213
US 2002087012	A1	20020704	US 2001-35005	20011220
US 6855834	B2	20050215		
NZ 516299	Α.	20021220	NZ 2001-516299	20011220
HR 2002000005	A1	20030430	HR 2002-5	20020104
US 2003178295	A1	20030925	US 2003-361800	20030210
PRIORITY APPLN. INFO.:				A 20001228
				W 20010307
				A 20010308
				A 20010322
				A1 20011220
OTHER SOURCE(S):	CASI	REACT 135:6122	5; MARPAT 135:61225	

Saloni Sharma 06/19/2006

AB High-purity citalogram (I) is prepared on an industrial scale by: subjecting a citalogram precursor [II; Z = iodo, bromo, chloro, CF3(CF2)nSO2O; n = 0-8] (e.g., Z = Br) to a cyanide exchange reaction in which the group Z is exchanged with cyanide by reaction with a cyanide source (e.g., CuCN) in a solvent (e.g., sulfolane); the crude citalogram product is optionally subjected to some initial purification and the crude citalogram base is subsequently subjected to a thin- or falling-film distillation process.

II

IT 64169-39-7 64169-45-5 260066-78-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for the preparation of high-purity citalogram by cyanidation with purification via thin-film distillation)

RN 64169-39-7 CAPLUS

CN

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 64169-45-5 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

IT 64169-39-7, 1-(4-Fluorophenyl)-1-(3-dimethylaminopropyl)-5bromophthalane 64169-45-5, 1-(4-Fluorophenyl)-1-(3dimethylaminopropyl)-5-chlorophthalane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of citalopram by nickel-catalyzed cyanation of halo precursors)

RN 64169-39-7 CAPLUS
CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-

dimethyl- (9CI) (CA INDEX NAME)

64169-45-5 CAPLUS RN

1-Isobenzofuranpropanamine, 5-chloro-1-(4-fluorophenyl)-1,3-dihydro-N,N-CNdimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:489362 CAPLUS

DOCUMENT NUMBER:

135:61225

TITLE:

Process for the preparation of high-purity citalogram

by cyanidation with purification via thin-film

distillation

INVENTOR(S):

Castellin, Andrea; Volpe, Giulio; Sbrogio, Federico

PATENT ASSIGNEE(S):

H. Lundbeck A/s, Den.

SOURCE:

PCT Int. Appl., 10 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.				KIND DATE			APPLICATION NO.						DATE			
						_											
WO	2001	0478	77		A2		2001	0705	1	NO 2	001-	DK14	В		20	0010	307
WO	2001	0478	77		A3		2000:	1227									
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,
		HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,
		RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	ΤŻ,	UA,	UG,	US,	UZ,
		VN,	YU,	ZA,	ZW												
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		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
CA	2359	810			AA		2001	0705	(CA 2	001-	2359	810		20	0010	307
CA	2359	810			С		2002	1105									
ΑU	2001	1039202 A5			2001	0709		AU 2	001-	3920	2		20	0010	307		
ΑU	2001	1003	99		A4	A4 20011		1101		AU 2	001-	1003	99		20010307		
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ΕP	1181	272						0227	7 EP 2001-913727				20010307				

L45 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2001:592319 CAPLUS

Correction of: 2001:386023

DOCUMENT NUMBER:

135:137393

Correction of: 134:353251

TITLE:
INVENTOR(S):

Method for the preparation of citalopram Petersen, Hans; Rock, Michael Harold

PATENT ASSIGNEE(S):

H Lundbeck A/S, Den.

SOURCE:

Brit. UK Pat. Appl., 15 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	CENT I	NO.			KINI		APP	LIC	DATE									
	CD	2254	20.71	2001	0001		an	200		10001110									
	GB	2354	240			B2	2001	0523				_							
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	WO	2000	0119	26		A2	2000	0309		WO	199	9-1	DK64:	3		19991119			
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						B2				JP	200	JU -	56/0	65		T	9991	TIA	
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		1105	384			T T3 B6 B	2002	0/31		EC FI	193	7 7 7	768Z	06		1	9991		
		2172	356 74			T3	2002	0310		ED CE	T 2 ;	フラー	⊅ 00∠	Ub			9991		
	-	2921	/4			B6	2003	1202		CZ	200) T =	317 0165	~ 0		19991119			
	CN	1129	593			В	2003	1203		CIA	193	99-	8TP\	19991119					

NZ 5	514982	Α	20040130	NZ	1999-514982		19991119
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CA 2	2290125	C	20040810				
NO 2	2001000318	A	20010220	NO	2001-318		20010119
SE 2	2001000194	A	20010425	SE	2001-194		20010124
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FI 2	2001000154	A	20010209	FI	2001-154		20010125
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ZA 2	2001007956	Α	20020927	z_{A}	2001-7956		20010927
ZA 2	2001008855	A	20020611	ZA	2001-8855		20011026
US 2	2002061925	A1	20020523	US	2001-12025		20011106
US 6	750358	B2	20040615				
BG 1	106190	A	20020830	BG	2001-106190		20011207
ZA 2	2002005023	Α	20030623	ZA	2002-5023		20020621
HK 1	L047745	A1	20040910	HK	2002-109330		20021224
PRIORITY	APPLN. INFO.:			DK	1999-921 .	Α	19990625
				WO	1999-DK643	W	19991119

OTHER SOURCE(S):

CASREACT 135:137393; MARPAT 135:137393

GI

AB A method for preparing the antidepressant, citalopram [I; R = CN], by reacting an isobenzofuranpropanamine [I; R = Cl or Br] with a cyanide source in the presence of a nickel catalyst is presented. Citalopram is produced in high yield as a very pure product using this catalytic process. Thus, sequential addition of I (R = Cl) and NaCN to the Ni catalyst formed by reflux of NiCl2 with PPh3 in AcCN in the presence of a catalytic amount of Zn, followed by workup and treatment with oxalic acid, gave citalopram oxalate in 55% yield.

IT 59729-33-8P 128196-01-0P, (S)-Citalopram

207559-01-1P, Citalopram oxalate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

Ι

(preparation of citalogram by nickel-catalyzed cyanation of halo precursors) 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN

GB 2365865 US 2002025982 US 6426422	B2 A1 B2	20020717 20020228 20020730	US 2001-930107	20010814			
US 2002026062 US 6509483	A1 B2	20020730 20020228 20030121	US 2001-930110	20010814			
WO 2002016341	A1	20020228	WO 2001-DK541	20010814			
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GM, HR,	HU, ID,	IL, IN, IS,	JP, KE, KG, KP, KR, KZ,	LC, LK, LR,			
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RW: GH, GM,	KE, LS,	MW, MZ, SD,	SL, SZ, TZ, UG, ZW, AT,	BE, CH, CY,			
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RO, RU,	SD, SE,	SG, SI, SK,	SL, TJ, TM, TR, TT, TZ,	UA, UG, US,			
UZ, VN,							
RW: GH, GM,	KE, LS,	MW, MZ, SD,	SL, SZ, TZ, UG, ZW, AT,	BE, CH, CY,			
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GR 1004074	B2	20021126					
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EP 1309581	A1	20030514	EP 2001-957785	20010814			
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AU 2001100271	B4		GR 2021 2052	20010015			
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CZ 295863	· B6		CZ 2001-2959	20010815			
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Saloni Sharma 06/19/2006

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PRIORITY APPLN. INFO.:
                                             DK 2000-1231
                                                                  A 20000818
                                             WO 2001-DK541
                                                                     20010814
                                             WO 2001-DK542
                                                                  W 20010814
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OTHER SOURCE(S):

CASREACT 137:78853

AB Citalopram (I) was prepared by converting a 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran to the 5-carboxylic acid derivative and converting the latter to I. Thus, 5-bromo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran in Me3COMe at -78° was treated with BuLi followed by stirring for 2 h at -30°. Solid CO2 was added followed by stirring for 16 h at room temperature to give 5-carboxy-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran. The latter was heated with sulfamide and SOCl2 in sulfolane at 130° for 2 h to give I.

IT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Citalopram from 5-halo-1-(4-fluorophenyl)-1-(3-dimethylaminopropyl)-1,3-dihydroisobenzofuran)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

AB Citalopram and other phthalanes I [R1 = CN, R2 = halogen, trifluoromethyl, CN, acyl] are made by treating a salt of I [R1 = halogen] with cuprous cyanide. Thus, 100g I.oxalate [R1 = Br, R2 = F] was treated with 35 g CuCN in diglyme at 150-155° for 3 h to give 35 g I [R1 = CN, R2 = F] as the hydrobromide.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P, Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (preparation of phthalanes)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

$$O$$
 (CH₂)₃-NMe₂

HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64372-43-6

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of phthalanes)

RN 64372-43-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2002:550142 CAPLUS 137:78853

DOCUMENT NUMBER: TITLE:

Preparation of Citalopram from 5-halo-1-(4fluorophenyl) -1-(3-dimethylaminopropyl) -1,3-

dihydroisobenzofuran.

INVENTOR(S):

Petersen, Hans; Ahmadian, Haleh

PATENT ASSIGNEE(S):

H. Lundbeck A/S, Den.

SOURCE:

Patentschrift (Switz.), 15 pp.

CODEN: SWXXAS

DOCUMENT TYPE:

Patent LANGUAGE: German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 691969	A	20011215	CH 2001-1522	20010816
CA 2354880	AA	20020122	CA 2001-2354880	20010809
CA 2354880	C	20030603		
CA 2354877	AA	20020218	CA 2001-2354877	20010809
CA 2354877	С	20060502		
FI 2001001621	A	20020219	FI 2001-1621	20010809
FI 2001001622	A	20020219	FI 2001-1622	20010809
IL 144816	A1	20050925	IL 2001-144816	20010809
IT 2001MI1785	A1	20020218	IT 2001-MI1785	20010813
IT 2001MI1786	A1	20020218	IT 2001-MI1786	20010813
IN 194521	Α	20041113	IN 2001-MA665	20010813
GB 2362647	A1	20011128	GB 2001-19733	20010814
GB 2362647	B2	20020918		
ZA 2001006687	Α	20020214	ZA 2001-6687	20010814
DK 200101216	A5	20020219	DK 2001-1216	20010814
DK 200101219	A5	20020219	DK 2001-1219	20010814
NO 2001003942	Α	20020219	NO 2001-3942	20010814
NO 2001003943	Α	20020219	NO 2001-3943	20010814
GB 2365865	A1	20020227	GB 2001-19734	20010814

ACCESSION NUMBER:

2002:695968 CAPLUS

DOCUMENT NUMBER:

137:216863

TITLE:

Preparation of phthalanes

INVENTOR(S):

Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao;

Rao, Dhanmaraj Ramachandra

PATENT ASSIGNEE(S):

Cipla Ltd., India; Wain, Christopher Paul

SOURCE:

PCT Int. Appl., 11 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

Ι

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT	NO.			KIND DATE					APPL	ICAT		DATE					
WO	2002	A1		2002	0912		WO 2	002-		20020307								
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							FR,											
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CA	2442	613			AA		2002	0912		CA 2	002-		20020307					
EP	EP 1366034				A1 20031203					EP 2	002-							
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RU	2276	148			C2		2006	0510		RU 2	003-		20020307					
	5167				В		2004											
BG	1082	32			Α		2005	0430		BG 2	003-		20031006					
r_{Λ}	1313	2			В		2004	0620		LV 2	003-		20031007					
ZA	2003	0080			Α		2004	1117					20031016					
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US	6903	228			B2		2005	0607										
PRIORIT	Y APP	LN.	INFO	.:					1	GB 2	001-	5627			A 2	0010	307	
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OTHER SO	OTHER SOURCE(S): GI					REAC	T 13	7:21	6863	; MA	RPAT	137	:216	863				

$$R^1$$
 O
 $(CH_2)_3NMe_2$

$$^{\text{NC}}$$
 $^{\text{O}}$ $^{\text{CH}_2)_3-\text{NMe}_2}$

HBr

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

IT 64169-39-7 260066-78-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyanation process for the preparation of citalogram from)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 260066-78-2 CAPLUS

CN 1-Isobenzofuranpropanamine, 1-(4-fluorophenyl)-1,3-dihydro-5-iodo-N,N-dimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

Bakthavathsalan

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA	TENT	NO.			KIND DATE					ICAT:		DATE						
WO	WO 2002072565					_	20020919						20020308					
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CA	2439		•		•	-	2002											
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CN	1496	•	•		•		2004	•	•	-		8061	16		2	0020	308	
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	JP 2005500256																	
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PRIORIT											001-					0010		
	RIORIII AIIM. INFO										002-			-		0020		
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OTHER SOURCE(S): CASREACT 137:232543

AB An improved and industrially advantageous process for the preparation of citalopram and pharmaceutically acceptable acid addition salts consists of reacting a precursor substituted with a bromo or an iodo group in the same position as the cyano group in citalopram with a cyanide source in a solvent in the present of a N-containing base; the citalopram free base may then be salified with a pharmaceutically acceptable acids.

IT 59729-32-7P, Citalopram hydrobromide 59729-33-8P,

Citalopram

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(cyanation process for the preparation of citalogram)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

Saloni Sharma 06/19/2006

ΙT 64372-43-6 479065-02-6

RL: RCT (Reactant); RACT (Reactant or reagent) (process for the preparation of citalogram)

RN64372-43-6 CAPLUS

1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-CN dimethyl-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 64169-39-7 CMF C19 H21 Br F N O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 479065-02-6 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl-, hydrobromide (9CI) (CA INDEX NAME)

HBr

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:716262 CAPLUS

DOCUMENT NUMBER: 137:232543

TITLE: Cyanation process for the preparation of citalogram INVENTOR(S): Biswas, Sujay; Sharma, Tarun Kant; Kumar, Yatendra;

Sathyanarayana, Swargam; Vijayaraghavan,

AB An improved process for the preparation of citalopram via substitution of the halogen of halophthalane salts I (R = halogen; X = oxalate, fumarate, maleate, citrate, acetate, formate, hydrochloride, hydrobromide, sulfate) using cuprous cyanide in an organic solvent. Thus, bromophthalane oxalate I (R = Br, X = oxalate) was reacted CuCN in diglyme under a nitrogen atmospheric

at 150-155° for 3 h to form citalopram which was converted to its HBr

salt I (R = CN, X = HBr).
IT 59729-33-8P, (±)-Citalopram
RL: IMF (Industrial manufacture); RCT (Reactant); SPN

(Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for the preparation of citalogram)

Ι

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 59729-32-7P, (\pm) -Citalopram hydrobromide 85118-27-0P, (\pm) -Citalopram hydrochloride 207559-01-1P, (\pm) -Citalopram oxalate

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for the preparation of citalogram)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

NC
$$O$$
 (CH₂)₃-NMe₂

• HBr

RN 85118-27-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

Saloni Sharma

A novel method is provided for the manufacture of the antidepressant AB escitalopram, i.e., (S)-I. The method comprises chromatog. separation of the enantiomers of either (1) citalogram, i.e., (\pm) -I, or (2) an intermediate in its production, using a chiral stationary phase such as Chiralpak AD or Chiralcel OD. Novel chiral intermediates for the synthesis of escitalopram, made by said method, are also provided. example, the intermediate nitrile diol (±)-II was resolved using Chiralpak AD stationary phase on a Novasep Licosep 10-50 simulated moving bed chromatograph with MeCN mobile phase at 30°, to give both enantiomers of II with purity exceeding 99% ee. Similarly resolved in 96-99% yield and >99% ee were bromide diol (±)-III and bromophthalane (±)-IV, using Chiralpak AD and Chiralcel OD, resp. Resolution of (±)-IV was performed on a 500-g scale using 98:2 isohexane/isopropanol (vol/vol), and also on a smaller scale using supercrit. CO2 with MeOH/Et2NH/CF3CO2H modifier. The obtained bromide (S)-(+)-IV underwent cyanation by Zn(CN)2 and Pd(PPh3)4 according to the method of WO 00/13648, giving escitalopram in 80% yield and 99.6% ee.

IV

IT 488148-14-7P, (S)-(+)-1-(4-Fluorophenyl)-1-[3-

(dimethylamino)propyl]-5-bromophthalane

RL: PUR (Purification or recovery); RCT (Reactant); PREP

(Preparation); RACT (Reactant or reagent)

(intermediate enantiomer; preparation of escitalopram via chromatog. resolution

of citalopram or intermediates using carbohydrate-based chiral stationary phases) $\,$

RN 488148-14-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

128196-01-0P, Escitalopram IT

> RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(preparation of escitalopram via chromatog, resolution of citalopram or intermediates using carbohydrate-based chiral stationary phases)

RN 128196-01-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2006 ACS on STN L45 ANSWER 15 OF 25

ACCESSION NUMBER:

2003:8116 CAPLUS

DOCUMENT NUMBER:

138:55857

TITLE:

Process for the preparation of citalogram

INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra

PATENT ASSIGNEE(S):

Cipla Limited, India

SOURCE:

Brit. UK Pat. Appl., 11 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
GB 2376945	A1	20021231	GB 2001-15708	20010627		
PRIORITY APPLN. INFO.:			GB 2001-15708	20010627		
OTHER SOURCE(S):	CASRE	ACT 138:55857	; MARPAT 138:55857			

GI

CM 2

CRN 64-19-7 CMF C2 H4 O2

TT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); RCT (Reactant); SPN

(Synthetic preparation); PREP (Preparation); RACT (Reactant

or reagent)

(improved process for the manufacture of citalopram hydrobromide from 5-bromophthalide)

RN 59729-33-8 CAPLUS

5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-CN

fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7P, 1-(4-Fluorophenyl)-1-(3-dimethylamino-propyl)-5-

bromophthalane

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation and cyanation of; improved process for the manufacture of citalopram

hydrobromide from 5-bromophthalide)

RN64169-39-7 CAPLUS

CN1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,Ndimethyl- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2003:58074 CAPLUS

DOCUMENT NUMBER:

138:122548

TITLE:

Method for the preparation of escitalopram via chromatographic resolution of citalopram or its intermediates using carbohydrate-based chiral

Qazi 10/500,532 Page 50

stationary phases

INVENTOR(S):

Bech Sommer, Michael; Nielsen, Ole; Petersen, Hans; Ahmadian, Haleh; Pedersen, Henrik; Brosen, Peter; Geiser, Fiona; Lee, James; Cox, Geoffey; Dapremont, Olivier; Suteu, Christina; Assenza, Sebastian P.;

Hariharan, Shankar; Nair, Usha

PATENT ASSIGNEE(S):

SOURCE:

H. Lundbeck A/S, Den. PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO. KIND DATE						APPLICATION NO.						DATE					
WO	WO 2003006449			A1 20030123								20020712						
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		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE	, KG,	KP,	KR,	KZ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	· MD,	MG,	MK,	MN	, MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK	, SL,	TJ,	TM,	TN,	TR,	TT,	TZ,	
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		CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR	, GB,	GR,	IE,	IT,	LU,	MC,	NL,	
		PT,	SE,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI	, CM,	GA,	GN,	GQ,	GW,	ML,	MR,	
		NE,	SN,	TD,	TG													
CA	2451	124			AA	AA 20030123			CA 2002-2451124						20020712			
EP	1409	472			Al	A1 20040421		EP 2002-750836					20020712					
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BR	BR 2002010817			A	2004	0622		BR :	2002-	1081	20020712							
CN	CN 1527825			A	2004	0908		CN :	2002-	8139	20020712							
JP	JP 2004538276 T2				20041224 JP 2003-51222						21	20020712						
								ZA 2003-9471					20031205					
	1085				Α		2005	0331		BG :	2004-	1085	72		2	0040	209	
US	2005	0652	07		A1		2005	0324		US :	2004-	4838	24		2	0040	930	
PRIORIT	Y APP	LN.	INFO	. :						DK :	2001-	1101			A 2	0010	713	
										DK :	2001-	1851			A 2	0011	211	
										DK :	2001-	1852			A 2	0011	211	
										WO :	2002-	DK49	1	1	W 2	0020	712	

OTHER SOURCE(S): CASREACT 138:122548

GI

HBr

RN 207559-01-1 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 500733-84-6 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.:

US 2001-315391P P 20010828
OTHER SOURCE(S):

CASREACT 138:221462; MARPAT 138:221462
GI

AB A process for the preparation of 1-(4'-fluorophenyl)-1-(3-dimethylamino-propyl)-

5-phthalanecarbonitrile (I), or a pharmaceutically acceptable salt thereof, comprising performing two successive Grignard reactions on 5-bromophthalide, wherein the 5-bromophthalide is reacted with the first Grignard reagent in the presence of a Lewis acid, so reducing byproduct formation and improving yields. Also claimed is a process for the preparation of aryl ketone II [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl, optionally containing one heteroatom; W = haloge, CN, OH, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl, aralkyl; n = 0 - 4] which comprises the step of reacting a phthalide III with a Grignard reagent, R1MgY (Y = halogen) and is characetrized in that the phthalide is reacted with a Lewis acid to form an adduct prior to reaction with the Grignard reagent. Thus,.

59729-32-7P, Citalopram hydrobromide 207559-01-1P, Citalopram oxalate 500733-84-6P; Citalopram acetate RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(improved process for the manufacture of citalogram hydrobromide from 5-bromophthalide)

RN 59729-32-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, monohydrobromide (9CI) (CA INDEX NAME)

Qazi 10/500,532 Page 76

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MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              CA 1999-2353618
     CA 2353618
                           AA
                                  20000615
                                                                        19991203
                                               BR 1999-16873
     BR 9916873
                           Α
                                  20010821
                                                                        19991203
                                               EP 1999-957263
     EP 1137644
                           A1
                                  20011004
                                                                        19991203
     EP 1137644
                           В1
                                  20030910
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     TR 200101605
                           T2
                                  20011022
                                               TR 2001-200101605
                                                                        19991203
     JP 2002531556
                           T2
                                  20020924
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                           Α
                                  20030926
                                               NZ 1999-511751
                                                                        19991203
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                           \mathbf{T}
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                                                                        19991203
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                           A1
                                  20040620
                                               IL 1999-143082
                                                                        19991203
     ZA 2001003987
                                  20020516
                                               ZA 2001-3987
                           Α
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     HR 2001000418
                           A1
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                                               HR 2001-418
                                                                        20010601
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                           A1
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                                               US 2001-874392
                                                                        20010604
     NO 2001002802
                           Α
                                  20010807
                                               NO 2001-2802
                                                                        20010607
     BG 105646
                                  20020228
                                               BG 2001-105646
                           Α
                                                                        20010625
     HK 1043121
                                  20051216
                                               HK 2002-104563
                           A1
                                                                        20020619
PRIORITY APPLN. INFO.:
                                               US 1998-111360P
                                                                    Ρ
                                                                        19981208
                                               DK 1998-1631
                                                                     Α
                                                                        19981209
                                               WO 1999-DK676
                                                                     W
                                                                        19991203
                                                                    Α
                                               US 2000-632117
                                                                        20000803
                                               WO 2001-US23487
                                                                        20010726
OTHER SOURCE(S):
                          MARPAT 133:43427
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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AB The title compds. [I; R1 = H, halo, CF3, etc.; R2, R3 = H, CF3, alkyl, etc.; n = 1-5; m = 0-1; A = N(R4)DsZq, II-IV (wherein Z = O, S; s = 0-1; q = 0-1; R4 = H, alkyl, alkenyl, etc.; D = alkylene, alkenylene, alkynylene); B = (un)substituted Ph, indolyl, etc.; Ar = (un)substituted Ph, thienyl, furanyl, etc.] and their pharmaceutically acceptable acid addition salts which are potently binding to the 5-HT1A receptor, were prepared Thus, reacting 5-(4-bromobutyl)-1,4-benzodioxane (preparation given) with (+)-1-[3-(methylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile in the presence of K2CO3 in Me iso-Bu ketone afforded 73% (+)-V which showed IC50 of 39 nM against 3H-5-CT binding and IC50 of 60 nM against serotonin reuptake.
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IT 274908-99-5P 274909-01-2P 274909-03-4P 274909-05-6P 274909-07-8P 274909-08-9P 274909-09-0P 274909-11-4P 274909-17-0P 274909-28-3P 274909-26-1P 274909-27-2P 274909-28-3P 274909-29-4P 274909-30-7P 274909-31-8P 274909-32-9P 274909-33-0P 274909-34-1P 274909-35-2P 274909-36-3P 274909-37-4P 274909-38-5P 274909-39-6P 274909-40-9P 274909-41-0P 274909-42-1P 274909-43-2P
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Saloni Sharma 06/19/2006

halophthalane in the corresponding Grignard reagent; this intermediate product may be converted into citalopram via intermediate formation of an aldehyde and in the subsequent transformation of the functional group via oxime or hydrazone; or else be converted into citalopram via reaction with compds. containing a cyano group bound to a leaving group. The process described makes it possible to obtain citalopram in high yields, and does not involve the use of drastic conditions of temperature

IT **59729-33-8P**, Citalopram

RL: IMF (Industrial manufacture); PREP (Preparation) (process for synthesis of citalogram)

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

IT 64169-39-7D, Grignard compound

RL: RCT (Reactant); RACT (Reactant or reagent)
 (process for synthesis of citalogram)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

L45 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

2000:401811 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

133:43427

TITLE:

Preparation of benzofurans as 5-HT1A receptor ligands Andersen, Kim; Rottlander, Mario; Bogeso, Klaus Peter; Pedersen, Henrik; Ruhland, Thomas; Dancer, Robert

PATENT ASSIGNEE(S):

H. Lundbeck A/S, Den.

SOURCE:

PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.			KIND DATE				APPLICATION NO.							DATE		
							•									
WO 2000034263				ΑI	A1 20000615		WO 1999-DK676						19991203			
W :	AE,	AL,	AM,	AT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,
	DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,
	JP,	ΚĒ,	KG,	KΡ,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,

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274909-44-3P 274909-45-4P 274909-48-7P
     274909-49-8P 274909-50-1P 274909-51-2P
     274909-52-3P 274909-53-4P 274909-54-5P
     274909-55-6P 274909-57-8P 274909-58-9P
     274909-59-0P 274909-60-3P 274909-61-4P
     274909-62-5P 274909-63-6P 274909-64-7P
     274909-65-8P 274909-66-9P 274909-67-0P
     274909-68-1P 274909-69-2P 274909-70-5P
     274909-71-6P 274909-72-7P 274909-73-8P
     274909-74-9P 274909-75-0P 274909-76-1P
     274909-77-2P 274909-78-3P 274909-79-4P
     274909-80-7P 274909-81-8P 274909-82-9P
     274909-83-0P 274909-84-1P 274909-85-2P
     274909-87-4P 274909-89-6P 274909-91-0P
     274909-93-2P 274909-94-3P 274909-95-4P
     274909-96-5P 274909-97-6P 274909-98-7P
     274909-99-8P 274910-00-8P 274910-01-9P
     274910-02-0P 274910-03-1P 274910-04-2P
     274910-05-3P 274910-06-4P 274910-07-5P
     274910-08-6P 274910-09-7P 274910-10-0P
     274910-11-1P 274910-12-2P 274910-13-3P
     274910-15-5P 274910-17-7P 274910-52-0P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation);
     USES (Uses)
        (preparation of benzofurans as 5-HT1A receptor ligands)
RN
     274908-99-5 CAPLUS
CN
     5-Isobenzofurancarbonitrile, 1-[3-[[4-(2,3-dihydro-1,4-benzodioxin-5-
     yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)- (9CI)
     (CA INDEX NAME)
```

Absolute stereochemistry. Rotation (+).

NC
$$Me$$
 $(CH_2)_3$ $(CH_2)_4$ O

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RN 274909-01-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-
yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1S)-,
ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-00-1
CMF C30 H31 F N2 O3
```

Absolute stereochemistry.

NC
$$Me$$
 $CH_2)_3$ $CH_2)_3$

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-03-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,3-dihydro-1,4-benzodioxin-5-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-02-3 CMF C29 H29 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-05-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[(2,3-dihydro-1,4-benzodioxin-5-yl)methyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274909-04-5 CMF C28 H27 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274909-07-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(2-methoxyphenoxy)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} & \text{MeO} \\ \hline \\ & \text{(CH}_2)_3 - \text{N-CH}_2 - \text{CH}_2 - \text{O} \\ \hline \\ & \text{F} \end{array}$$

RN 274909-08-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-methoxyphenoxy)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{NC} & \text{Me} \\ \hline \\ \text{(CH$_2$)} & \text{3-N-CH$_2$-CH$_2$-O} \\ \hline \\ \text{F} \end{array}$$

RN 274909-09-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[4-(1H-indol-3-yl)butyl]methylamino]propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_{4}^{H}$$

$$(CH_2)_{3}^{G}$$

$$(CH_2)_{3}^{G}$$

RN 274909-11-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]methylamino]propyl]-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

$$(CH_2)_{3}^{H}$$

$$(CH_2)_{3}^{O}$$

$$(CH_2)_{3}^{O}$$

RN 274909-17-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-chlorophenyl)-1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-yl)propyl]methylamino]propyl]-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274909-23-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(1H-indol-3-yl)ethyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 274909-24-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-

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methoxyphenyl)ethyl]methylamino]propyl] - (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{NC} \\ \text{O} \\ \text{(CH}_2)_3 - \text{N-CH}_2 - \text{CH}_2 \end{array} \\ \text{OMe} \\ \\ \end{array}$$

RN 274909-25-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, '1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(3-methoxyphenyl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH=CH_2$$
 $CH_2-CH_2-CH_2$ OME

RN 274909-26-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(2-methoxyphenyl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-27-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,5-dimethoxyphenyl)ethyl]methylami no]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{OMe} \\ \end{array}$$

RN 274909-28-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(2,5-dimethoxyphenyl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH=CH_2$$
 $CH_2-CH_2-CH_2$ OMe

RN 274909-29-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl(2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-30-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(1H-indol-3-yl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

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$$H_2C = CH - CH_2$$
 $CH_2 - CH_2 - N - (CH_2)_3$
 CN

RN 274909-31-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[(2-phenoxyethyl)-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-32-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenyl)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{NC} & \text{Me} & \text{MeO} \\ \hline \\ \text{(CH2)} \ 3 - \text{N- (CH2)} \ 3 \\ \hline \\ \text{F} \end{array}$$

RN 274909-33-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenyl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH=CH_2$$
 CH_2 $CH_$

RN 274909-34-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenyl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH$$
 CH_2 C

RN 274909-35-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenoxy)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

NC Me MeO (CH₂)
$$_3$$
 N- (CH₂) $_3$ - O

RN 274909-36-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(2-methoxyphenoxy)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH$$
 CH_2 C

RN 274909-37-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenoxy)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$Me$$
 $(CH_2)_3 - N - (CH_2)_3 - O$ OMe

RN 274.909-38-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(3-methoxyphenoxy)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

NC
$$CH_2-CH=CH_2$$
 CH_2 $CH_$

RN 274909-39-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[2-(phenylmethoxy)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-40-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(phenylmethoxy)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-41-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-

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indol-3-yl)propyl]methylamino]propyl]- (9CI) (CA INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-42-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$
 $(CH_2)_3 - N - (CH_2)_3$
 CN

RN 274909-43-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl]-2-propynylamino]propyl]- (9CI) (CA INDEX NAME)

HC
$$\equiv$$
 C-CH₂

$$(CH2)3-N-(CH2)3$$

$$CN$$

RN 274909-44-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

Me
$$CH_2-CH_2-N-(CH_2)_3$$
 CN

RN 274909-45-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-fluoro-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
 & \text{Me} \\
\hline
 & \text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_3 \\
\hline
 & \text{NH} \\
\end{array}$$
CN

RN 274909-48-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[3-(5-methyl-1H-indol-3-yl)propyl]amino]propyl]- (9CI) (CA INDEX NAME)

Me (CH₂) 3-N- (CH₂) 3
$$\stackrel{\text{Me}}{\longrightarrow}$$
 CN

RN 274909-49-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-50-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Me
$$CH_2-CH_2-N-(CH_2)_3$$
 CN

RN 274909-51-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$
CN

RN 274909-52-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c}
\text{Me} \\
\text{(CH2)}_{3} - \text{N- (CH2)}_{3}
\end{array}$$

RN 274909-53-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-fluoro-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

F

$$CH_2-CH_2-N-(CH_2)_3$$
 N
 N
 H

RN 274909-54-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(7-fluoro-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c}
Et \\
CH_2-CH_2-N-(CH_2)_3
\end{array}$$
CN

RN 274909-55-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CFINDEX NAME)

C1

$$N_{H}$$
 N_{H}
 N_{H}

RN 274909-57-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[methyl[4-/ (5-methyl-1H-indol-3-yl)butyl]amino]propyl]- (9CI) (CA INDEX NAME)

Me
$$(CH_2)_4 - N - (CH_2)_3$$
 CN

RN 274909-58-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-methyl-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Me (CH₂)₃-N-(CH₂)₃

$$\stackrel{\text{Et}}{\underset{\text{H}}{\bigvee}}$$

CN

RN 274909-59-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(7-fluoro-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-60-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-fluoro-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-61-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1
$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

$$CN$$

RN 274909-62-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-chloro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

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$$\begin{array}{c|c} & & & \\ & & & \\ \hline \\ & & \\ &$$

RN 274909-63-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$C1 \xrightarrow{\text{Et}} CH_2 - CH_2 - N - (CH_2)_3 \xrightarrow{\text{CN}} CN$$

RN 274909-64-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

F
$$CH_2-CH_2-N-(CH_2)_3$$
 CN

RN 274909-65-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[4-(5-fluoro-1H-indol-3-yl)butyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

F

(CH₂)
$$_4$$

(CH₂) $_4$

(CH₂) $_3$

(CN

CN

RN 274909-66-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(5-chloro-1H-indol-3-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CAINDEX NAME)

C1
$$(CH_2)_4 - N - (CH_2)_3$$

$$CN$$

$$CN$$

RN 274909-67-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1

$$(CH_2)_3 - N - (CH_2)_3$$
 $(CH_2)_3 - N - (CH_2)_3$
 $(CH_2)_3 - N - (CH_2)_3$
 $(CH_2)_3 - N - (CH_2)_3$

RN 274909-68-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5,7-difluoro-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CFINDEX NAME)

F

(CH₂)₃-N-(CH₂)₃

$$\stackrel{\text{Et}}{\underset{\text{F}}{}}$$

CN

RN 274909-69-2 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Br
$$CH_2-CH_2-N-(CH_2)_3$$
 CN

RN 274909-70-5 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-bromo-1H-indol-3-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA

Br
$$(CH_2)_3 - N - (CH_2)_3$$
 CN

INDEX NAME)

RN 274909-71-6 CAPLUS
CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CFINDEX NAME)

Saloni Sharma 06/19/2006

Br
$$CH_2-CH_2-N-(CH_2)_3$$
 CN

RN 274909-72-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(5-bromo-1H-indol-3-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CAINDEX NAME)

Br
$$(CH_2)_4 - N - (CH_2)_3$$
 CN

RN 274909-73-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-bromo-1H-indol-3-yl)propyl]ethylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

Br
$$(CH_2)_3 - N - (CH_2)_3$$
 CN

RN 274909-74-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[2-(5-iodo-1H-indol-3-yl)ethyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Et} \\ \text{CH}_2\text{-CH}_2\text{-N-(CH}_2)_3 \\ \text{CN} \end{array}$$

RN 274909-75-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[ethyl[3-(5-iodo-1H-indol-3-yl)propyl]amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-76-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[2-[[4-(5-chloro-1H-indol-3-yl)butyl]methylamino]ethyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1

Me

$$(CH_2)_4 - N - CH_2 - CH_2$$
 O
 CN

RN 274909-77-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

F
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-78-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(7-chloro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & \text{Me} \\ \hline & \text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_4 \\ \hline & \text{Cl} \end{array}$$

RN 274909-79-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5-chloro-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

C1
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-80-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-(5-bromo-1H-indol-3-yl)ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

Br
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-81-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[methyl[2-(5-methyl-1H-indol-3-yl)ethyl]amino]butyl]- (9CI) (CA INDEX NAME)

Me
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-82-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[[2-(5-iodo-1H-indol-3-yl)ethyl]methylamino]butyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \\ \text{CH}_2 - \text{CH}_2 - \text{N} - \text{(CH}_2)_4 \\ \\ \text{N} \\ \text{H} \end{array}$$

RN 274909-83-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[4-[[2-[5-(1,1-dimethylethyl)-1H-indol-3-yl]ethyl]methylamino]butyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

t-Bu
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-84-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[4-[methyl[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl]amino]butyl]- (9CI) (CA INDEX NAME)

i-Pr
$$CH_2-CH_2-N-(CH_2)_4$$
 CN

RN 274909-85-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(5-methyl-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{H}_2\text{C} = \text{CH} - \text{CH}_2 \\ \text{CH}_2 - \text{CH}_2 - \text{N} - (\text{CH}_2)_3 \\ \text{N} \\ \text{H} \end{array}$$

RN 274909-87-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-fluoro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$CH_2 - CH_2 - N - (CH_2)_3$$

$$CN$$

RN 274909-89-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(7-fluoro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_{2}C = CH - CH_{2}$$

$$CH_{2} - CH_{2} - N - (CH_{2})_{3}$$

$$CN$$

RN 274909-91-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-93-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274909-94-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-chloro-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

C1

$$H_2C = CH - CH_2$$
 $CH_2 - CH_2 - N - (CH_2)_3$
 CN

RN 274909-95-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl]propylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

RN 274909-96-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[(1-methylethyl)[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274909-97-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(4-fluoro-7-methyl-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274909-98-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(4-chloro-7-methyl-1H-indol-3-yl)ethyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$C1$$
 $H_2C = CH - CH_2$
 $CH_2 - CH_2 - N - (CH_2)_3$
 CN
 Me

RN 274909-99-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-chloro-1H-indol-3-yl)propyl]-2-propenylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

C1

$$H_2C = CH - CH_2$$
 $CH_2)_3 - N - (CH_2)_3$
 CN

RN 274910-00-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[2-propenyl[2-(1H-pyrrolo[3,2-h]quinolin-3-yl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)

RN 274910-01-9 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(7-fluoro-1H-indol-3-yl)propyl](2-furanylmethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA INDEX NAME)

$$(CH_2)_3 - N - (CH_2)_3$$

$$CN$$

RN 274910-02-0 CAPLUS

CN 1H-Indole-7-carboxylic acid, 3-[4-[[3-[5-cyano-1-(4-fluorophenyl)-1,3-dihydro-1-isobenzofuranyl]propyl]-2-propenylamino]butyl]- (9CI) (CA INDEX NAME)

$$H_2C = CH - CH_2$$

$$(CH_2)_4 - N - (CH_2)_3$$

$$CO_2H$$

$$CO_2H$$

RN 274910-03-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl]propylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Br} \\ \text{CH}_2\text{-CH}_2\text{-N-} \text{(CH}_2)_3 \\ \text{N} \\ \text{H} \end{array}$$

RN 274910-04-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(1H-indol-3-yl)propyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & \text{PhO-} \text{ CH}_2\text{--} \text{CH}_2 \\ & & & \\ & & \\ & & & \\ & &$$

RN 274910-05-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-(5-methyl-1H-indol-3-yl)ethyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{PhO-CH}_2\text{-CH}_2\\ \text{Me} \\ \text{CH}_2\text{-CH}_2\text{-N-(CH}_2)} \\ \text{M} \end{array}$$

RN 274910-06-4 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-fluoro-1H-indol-3-yl)ethyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

RN 274910-07-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1-[3-[(2-furanylmethyl)[3-(1H-pyrrolo[3,2-h]quinolin-3-yl)propyl]amino]propyl]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274910-08-6 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[3-(5-methyl-1H-indol-3-yl)propyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{PhO-CH}_2 - \text{CH}_2 \\ \text{Me} \\ \text{N} \\ \text{H} \end{array}$$

RN 274910-09-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(5-fluoro-1H-indol-3-y1)propyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

RN 274910-10-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5,7-difluoro-1H-indol-3-yl)ethyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

RN 274910-11-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1-[3-[(2-furanylmethyl)[4-(1H-pyrrolo[3,2-h]quinolin-3-yl)butyl]amino]propyl]-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 274910-12-2 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-(4-fluorophenyl)-1,3-dihydro-1-[3-[[2-[5-(1-methylethyl)-1H-indol-3-yl]ethyl](2-phenoxyethyl)amino]propyl]- (9CI) (CA INDEX NAME)

RN 274910-13-3 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[2-(5-bromo-1H-indol-3-yl)ethyl](2phenoxyethyl)amino]propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA
INDEX NAME)

$$\begin{array}{c} \text{PhO-CH}_2\text{-CH}_2\\ \text{CH}_2\text{-CH}_2\text{-N-(CH}_2)_3\\ \text{N}\\ \text{H} \end{array}$$

RN 274910-15-5 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[4-(2,3-dihydro-1,4-benzodioxin-5-yl)butyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RN 274910-17-7 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-[[3-(2,3-dihydro-1,4-benzodioxin-5-yl)propyl]methylamino]propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 274910-16-6 CMF C30 H31 F N2 O3

CM 2

CRN 144-62-7 CMF C2 H2 O4

RN 274910-52-0 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[2-[[4-(5-bromo-1H-indol-3-yl)butyl]methylamino]ethyl]-1-(4-fluorophenyl)-1,3-dihydro-(9CI) (CA

INDEX NAME)

Br
$$(CH_2)_4 - N - CH_2 - CH_2$$
 CN

IT 274910-18-8P

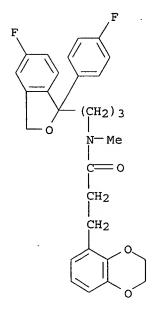
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(preparation of benzofurans as 5-HT1A receptor ligands)

RN 274910-18-8 CAPLUS

CN 1,4-Benzodioxin-5-propanamide, N-[3-[5-fluoro-1-(4-fluorophenyl)-1,3-dihydro-1-isobenzofuranyl]propyl]-2,3-dihydro-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:175646 CAPLUS

DOCUMENT NUMBER: 132:194283

TITLE: Method for the preparation of citalopram

INVENTOR(S): Petersen, Hans; Rock, Michael Harold; Svane, Henrik

PATENT ASSIGNEE(S): H. Lundbeck A/S, Den. SOURCE: PCT Int. Appl., 13 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

2

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2000013648 WO 2000013648	A2 2000031 A3 2000071	6 WO 1999-DK640 3	19991122
W: AE, AL, AM,	AT, AU, AZ, BA	, BB, BG, BR, BY, CA, CH,	CN, CU, CZ,
DE, DK, EE,	ES, FI, GB, GD	, GE, GH, GM, HR, HU, ID,	IL, IN, IS,
JP, KE, KG,	KP, KR, KZ, LC	, LK, LR, LS, LT, LU, LV,	MD, MG, MK,
		, RO, RU, SD, SE, SG, SI,	SK, SL, TJ,
		, VN, YU, ZA, ZW	
RW: GH, GM, KE,	LS, MW, SD, SL	, SZ, TZ, UG, ZW, AT, BE,	CH, CY, DE,
DK, ES, FI,	FR, GB, GR, IE	, IT, LU, MC, NL, PT, SE,	BF, BJ, CF,
CG, CI, CM,	GA, GN, GW, ML	, MR, NE, SN, TD, TG	
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	LV, FI, RO		
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				CA	1999-2290127	A3	19991122
				CN	1999-816751	Α	19991122
				GB	2001-1504	A3	19991122
				WO	1999-DK640	W	19991122

OTHER SOURCE(S):

CASREACT 132:194283; MARPAT 132:194283

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AB The title compound [I; R = CN], the well known antidepressant (no data), was prepared by reacting a compound I [wherein R = halo, CF3(CF2)nSO2; n = 0-8] with a cyanide source in the presence of a palladium catalyst and a catalytic amount of Cu+ or Zn2+, or with Zn(CN)2 in the presence of a palladium catalyst.

IT 59729-33-8P, Citalopram 207559-01-1P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(method for the preparation of citalogram)

Ι

RN 59729-33-8 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro- (9CI) (CA INDEX NAME)

RN 207559-01-1 CAPLUS

CN 5-Isobenzofurancarbonitrile, 1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 59729-33-8 CMF C20 H21 F N2 O

Saloni Sharma 06/19/2006

CM 2

CRN 144-62-7 CMF C2 H2 O4

IT 64169-39-7

RL: RCT (Reactant); RACT (Reactant or reagent) (method for the preparation of citalogram)

RN 64169-39-7 CAPLUS

CN 1-Isobenzofuranpropanamine, 5-bromo-1-(4-fluorophenyl)-1,3-dihydro-N,N-dimethyl- (9CI) (CA INDEX NAME)

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